VOLUME 79 • FEBRUARY 1958 • NUMBER 2

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Diagnosis of Cerebral Schistosomiasis
James F. Hammarsten

Use of Parenteral Diphenylhydantoin (Dilantin) Sodium in Control of Status Epilepticus
C. H. Carter

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L. Halpern, S. Feldman, and E. Peyser

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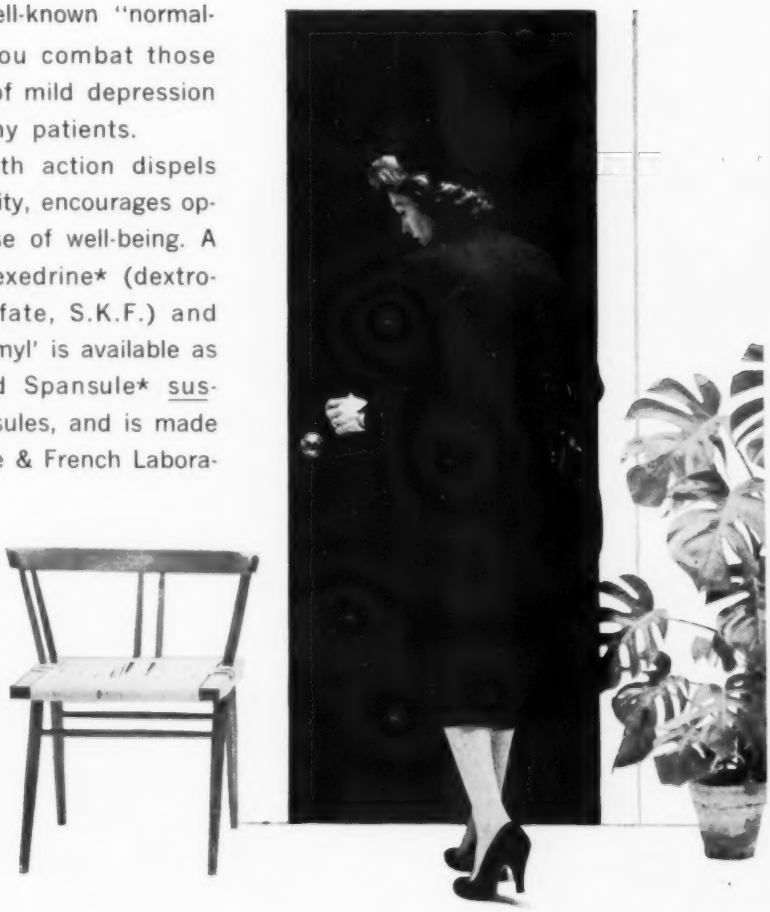

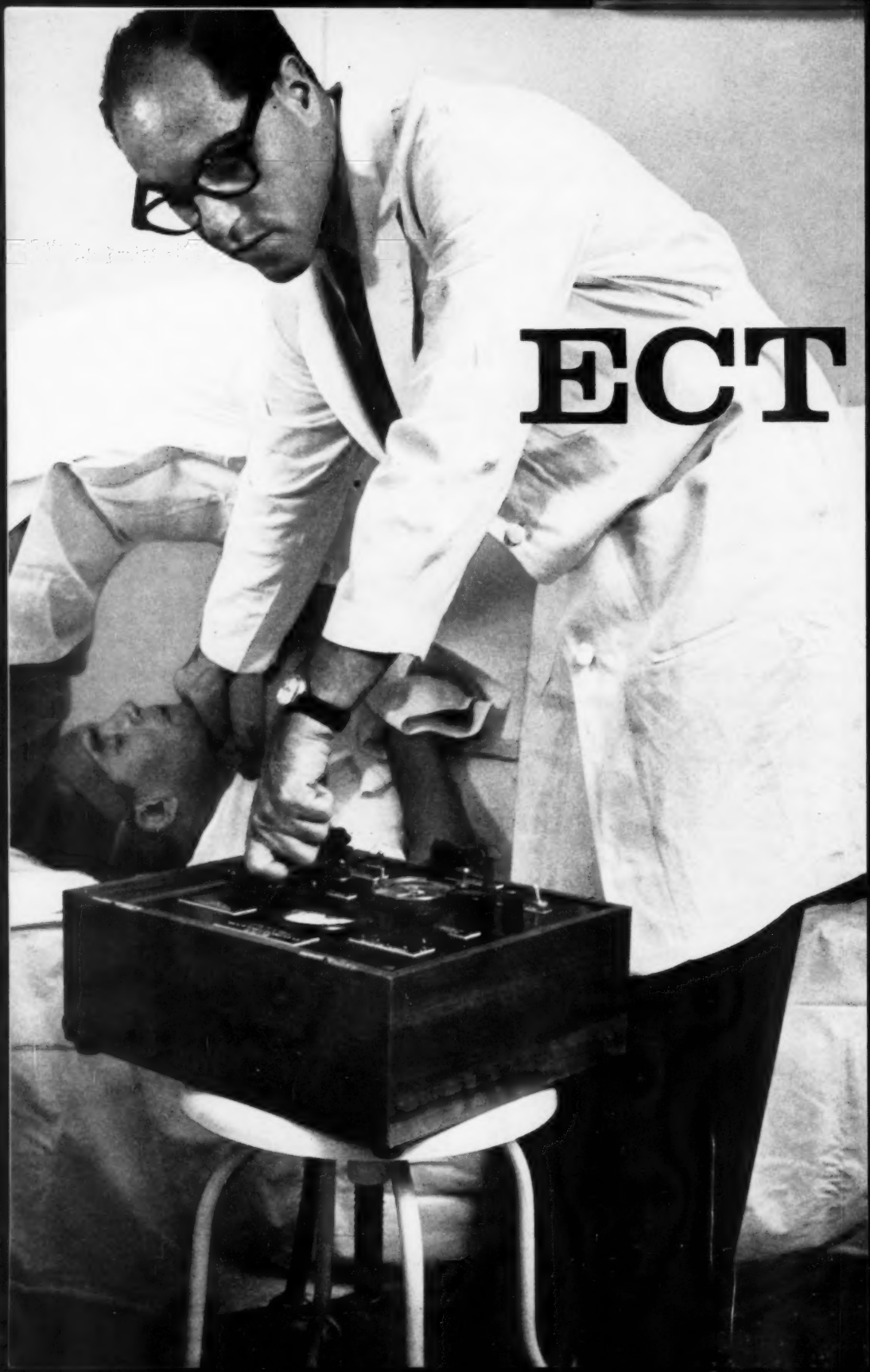
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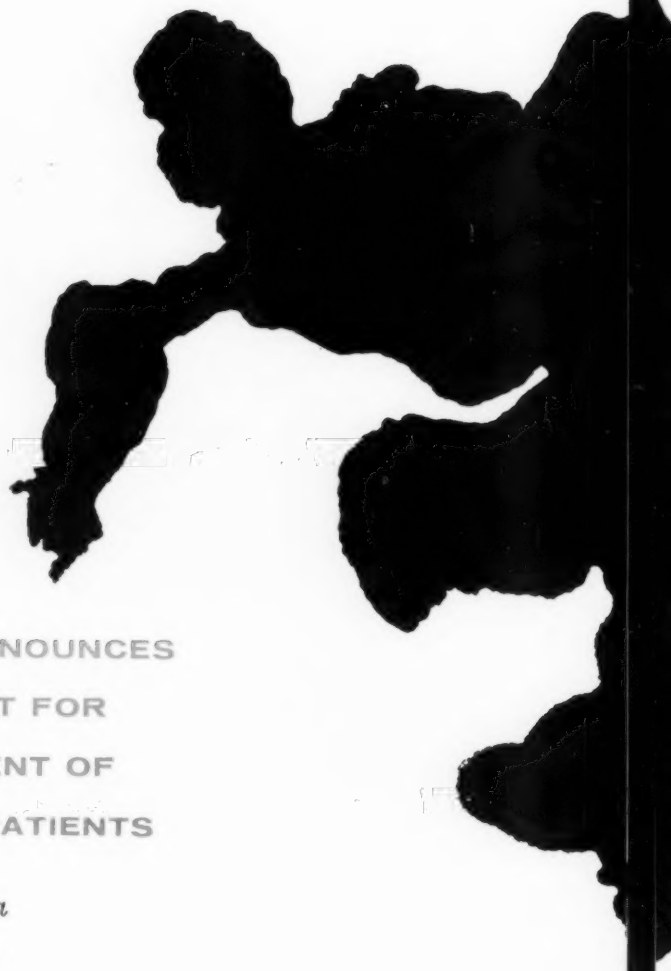

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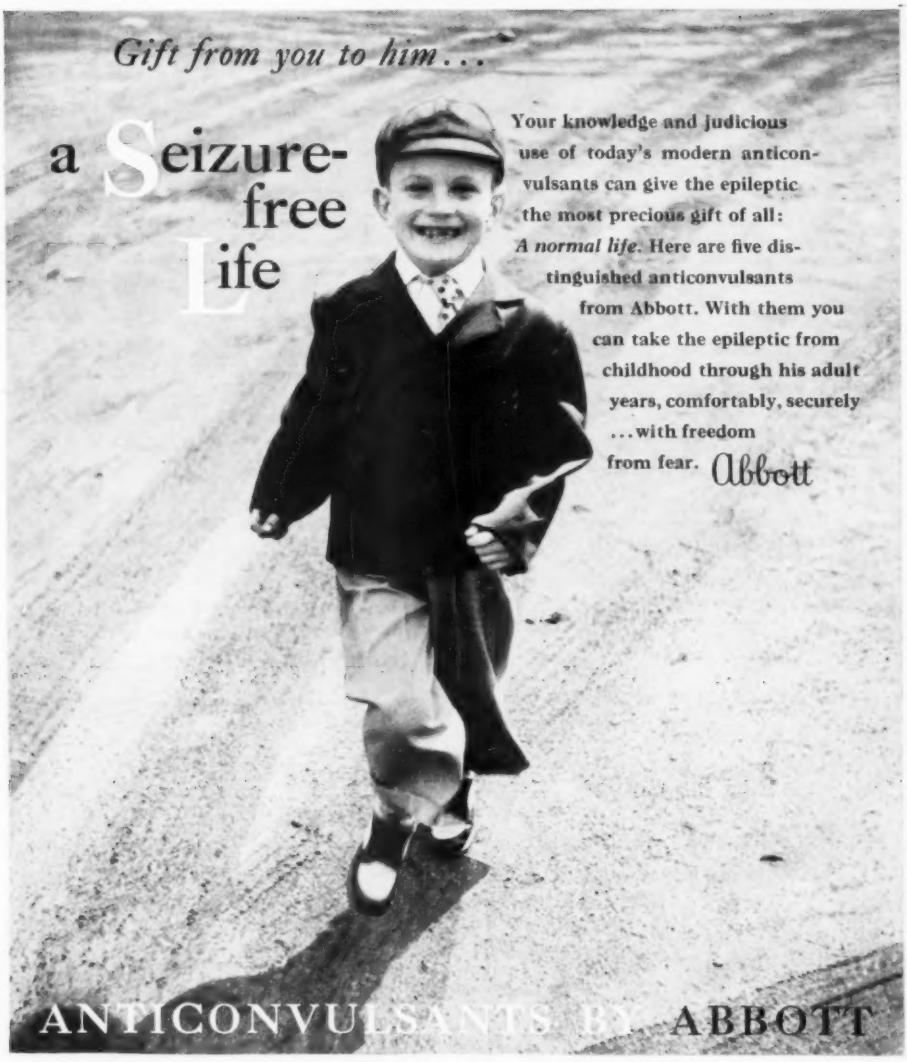
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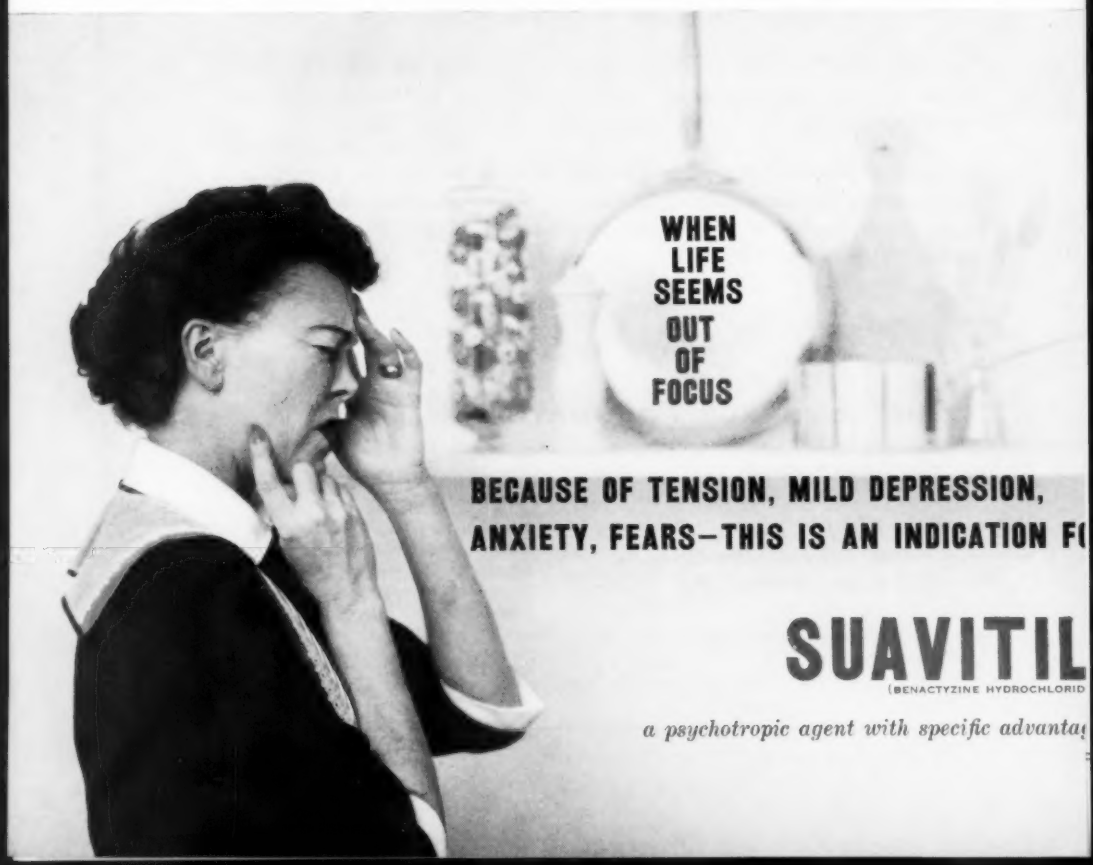

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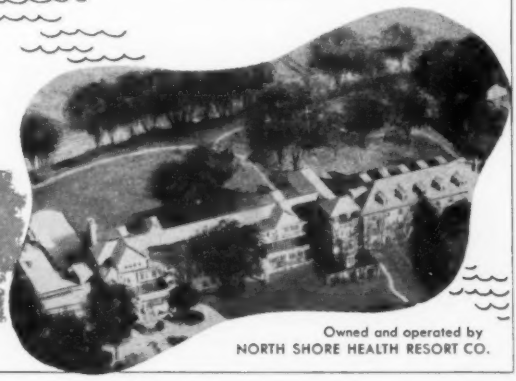

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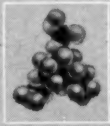

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Recessive Transmission to All Children by Parents Similarly Affected

A. S. DEKABAN, M.D., Bethesda, Md.

Mental deficiency is a heterogenous condition resulting from a variety of etiological factors. Even though in a considerable proportion of cases of mental deficiency we may have some insight into the underlying pathology and the cause, many other instances of this condition remain completely obscure.

A working classification of mental deficiency has been much in need for both practical and research purposes. Penrose [8] (1954) analyzed this aspect thoroughly and found that almost all suggested divisions of previous investigators were dichotomic, irrespective of what basis of classification was chosen. The following are the more interesting examples which he cites: "congenital" *vs.* "acquired"; "endogenous" *vs.* "exogenous"; "hereditary" *vs.* "acquired"; "pathological" *vs.* "subcultural." The last subdivision, which was presented by Lewis [6] in 1933, is the most comprehensive, and it will be used in this communication as a starting point in discussion, although in a modified version and wording.

It is suggested, then, that clinically all patients with mental defects may be divided into the following two groups:

1. Those who, in addition to mental deficiency, have abnormal neurological or laboratory findings. Here will belong all patients who have gross neurological deficits as a result of congenital malformation of the brain, cerebral birth injury, sequelae after encephalitis, and others, as well as the patients with known metabolic disorders, such as phenylpyruvic oligophrenia, galactosemia, or lipodosis. To determine the existence of such conditions a detailed clinical and psychological examination and various biochemical, serological, and other special procedures have to be performed. The last procedures may have to include electroencephalography, pneumoencephalography, arteriography, and, in special instances, brain biopsy.

2. Patients with mental defects in whom no significant clinical or laboratory abnormality could be detected in spite of an extensive search. The majority of patients belonging to this group have a milder form of mental deficiency and are also conveniently referred to in the medical literature as "undifferentiated" or "subcultural."

Although ultimately either environmental or genetic factors will be found responsible for mental deficiency in both groups, the inheritance of a responsible abnormal trait is numerically more frequent in the second group. An interesting family to be reported now belongs to the latter group, and the abnormality is inherited as a recessive trait. The propositus is one of the three children, all of whom are mental defectives.

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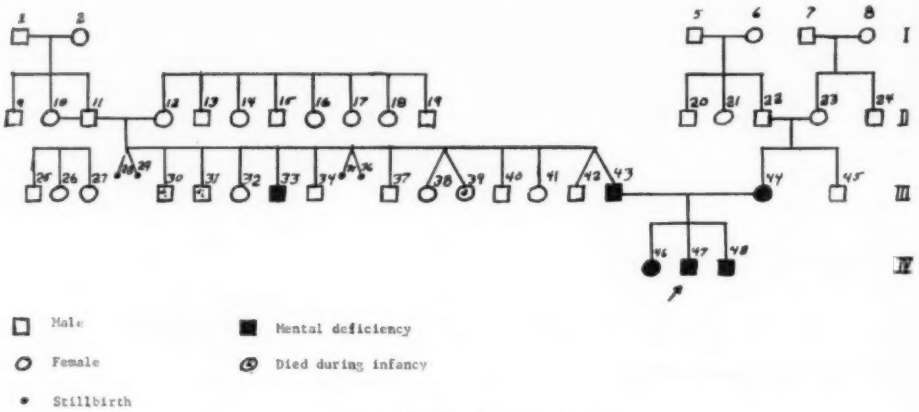

Fig. 1.—Pedigree of the L. family.

The L. Pedigree

IV 47 (Fig. 2).—Born in 1943. The pregnancy and birth were normal. Nothing unusual was noted in his general condition during the first four months of life. However, in the later stages of infancy it was noted that acquitition of milestones was retarded. He first sat up at 12 months of age, began to take steps when led at 20 months, and attempted to pronounce simple words, such as "dada" at 2½ years of age. Toilet habits were acquired at about 5 years of age. Infrequently he still has enuresis. His progress in walking was slow, and it was not until about 5 years of age that he walked alone confidently. At the age of 6 years he was rejected from public school because of very limited vocabulary and indistinct pronunciation. Subsequently, he was sent to a special school, where it was noted that his concentration span was very short and that he was very restless. When admonished, he would throw a tantrum spell. Finally he was rejected even from this school.

Psychological examination on Stanford-Binet Form L at the age of 7 years 10 months revealed his mental age to be four years, the I. Q. 51. Because of the low mental state of the parents and their inability to care for him at home, he was committed to a mental deficiency institution. There, he made a fair adjustment to the routine of the life, and his speech and motor development have slightly progressed.

The following are the findings on his recent hospitalization, at the age of 12 years: His height was 150 cm., which is normal for the age. The general physical development was normal (Fig. 2). The cardiovascular system, lungs, liver, spleen, and other internal organs were within normal limits. His vision, peripheral vision, fundi, hearing, and the rest of the cranial nerves were normal. His speech was indistinct, vocabulary very limited, and sentence construction poor. In fact, most of his sentences consisted of two, and occasionally of three, words. His attention and concentration were very short, and he became restless and nervous when kept at one task for more than a few minutes. Although there was no demonstrable muscular weakness, incoordination, or sensory impairment, the performance of skilled movements was deficient. This was evident during his dressing, manipulation of cubes, or running. The

Fig. 2.—Physical appearance of IV 47.

tendon reflexes were brisk and equal on the two sides, and the plantar reflexes were flexor.

In an attempt to obtain more information regarding the possible etiology of this condition, a variety of special tests were performed. Hematological examination gave normal results. Wassermann and Kahn tests were negative. Urinalysis was normal. Tests for phenylpyruvic acid, galactose, and toxoplasmosis were negative. Liver function tests, as well as the 24-hour urinary excretion of amino acids, were all within normal limits. Fasting blood sugar was normal. His and his mother's blood were Rh-positive. The cerebrospinal fluid constituents were in a normal range.

Radiographs of the chest, spine, and skull revealed normal structure, and there was no evidence of retarded maturation of bones. The formation f teeth was normal, and there was no evidence of growth disturbance of the facial bones on cephalometric examination. Head measurements: circumference, 54.1 cm.; length, 16.9 cm.; breadth, 13.8 cm.; height, 13.8 cm.; cephalic index, 0.81 cm.

Electroencephalographic tracings showed poorly organized background, with an abnormal amount of theta frequencies for his age. However, there was no evidence of focal abnormality or epileptiform activity. Psychological examination, using the Wechsler intelligence test for the child, at the age of 12 years revealed an over-all I. Q. of 50.

Fig. 3.—Pneumoencephalogram of V 47. The ventricular system is symmetrical and of approximately normal size. The subarachnoid space shows usual patterns.

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Pneumoencephalography (Fig. 3) showed that the ventricular system was of normal size and symmetry and the subarachnoid space of usual appearance and capacity.

Thus, the only positive findings of this rather extensive investigation were mental deficiency, defective speech, poor performance of skilled movements, and slight "immaturity" of electroencephalographic patterns.

IV 48.—Born in 1945. He is the younger brother of the patient just described. The course and length of the pregnancy were normal. No special difficulty at birth was encountered. His first months of life were normal; he slept well and presented no feeding problem. However, his subsequent development was grossly retarded. He began to walk at 3 years of age and said a few simple words at the age of 4 years. At 5 years of age he had bilateral purulent otitis media, which involved the inner ears. The infection has never cleared up completely and has left him deaf. The little speech that he had acquired was lost, and his mental development became more handicapped. He was hospitalized several times between his birth and 8 years of age for minor ailments, and a considerable amount of information regarding his development is available. At the age of 8 years, when he was committed to a mental deficiency institution, he was almost completely toilet-trained, although he still had occasional enuresis. He did not attempt to speak, nor was he able to hear. His motor performance, however, was fair.

While in this institution he became very dependent on his older brother, and they developed a form of pantomime language for daily life acts, which was not always understandable to observers. Unlike his brother, he has been particular about his clothing and has become very fond of mechanical games, such as arranging blocks, manipulating clocks, and the like.

Recently he was hospitalized, at the age of 10 years, for the purpose of complete investigation, including special tests. His height was 140 cm., and his build was normal (Fig. 4). All internal organs were found within normal limits. Both external ears were defectively formed. He was somewhat restless and quick-tempered but liked to play games, in particular, hiding. His span of attention, though better than his brother's, was considerably shorter than normal. There were large perforations in both eardrum membranes, which were partially filled with granulation tissue. A scanty purulent exudate was draining through the external auditory canal on both sides. No presence of hearing could be demonstrated by means of a ringing bell or shouting. The auropalpebral reflex was repeatedly negative. The caloric and rotation tests did not produce nystagmus, dizziness, or past pointing. Vision, perception

Fig. 4.—Physical appearance of IV 48. Both ears are malformed.

of smell and taste, and the rest of the cranial nerves were normal. He was using his eyesight with advantage to compensate for the lack of hearing and would perform a variety of tasks given in a way of pantomime. Motor system, sensation, and coordination were within normal limits, although skilled movements were somewhat deficient. His tendon reflexes were all brisk and equal, and plantar reflexes were flexor.

The following are the results of some of his psychological tests: At the age of 8 years he scored on the Kuhlmann Infant Scale, supplemented by Stanford-Binet Form L, a mental age of 2 years and an I. Q. of 25. Reexamination at the age of 10 years gave him an I. Q. of 38. Since in other psychological testing no consideration to his deafness was given, the scores were unjustly low and are not quoted here. Longer clinical observation of the patient gave some indication that even the two ratings quoted, in which some consideration to his deafness was given, might have been higher by several points.

Hematological examination and routine urinalysis were normal. Wassermann and Kahn tests were negative. Tests for toxoplasmosis, phenylpyruvic acid, and galactose, and the 24-hour urinary excretion of amino acids were all normal. Fasting blood sugar and liver function tests were within normal limits. The cerebrospinal fluid constituents were normal. The patient's and his mother's blood were Rh-positive.

X-ray examination of the chest, spine, and skull gave normal findings. The structure and the state of maturation of long bones were within normal limits. Dental examination and cephalometric x-ray assessment of teeth and mouth gave normal findings. Head measurements: circumference, 52.3 cm.; length, 16.7 cm.; breadth, 13.1 cm.; height, 13.4 cm.; cephalic index, 0.78 cm.

The electroencephalogram revealed poorly regulated background activity, with only a small amount of alpha rhythm at 8 cps. Anteriorly, irregular slow waves intermixed with fast activity of 22-24 cps were noted. However, there was no evidence of focal abnormality or epileptiform activity. For the patient's age the record was considered as mildly abnormal, of diffuse character. Intermittent loud acoustic stimuli did not evoke startle patterns.

The pneumoencephalogram (Fig. 5) showed a slightly enlarged ventricular system and normal subarachnoid space.

IV 46.—Born in 1934. She is the oldest and only sibling of the two brothers described above. The pregnancy and birth were uneventful. Her general development was first noted to be slow toward the end of the first year of life. She began to walk at 2 years of age and to say a few simple words at 3 years. Her vocabulary and ability to learn were so deficient that she was excluded from public schools as not capable of profiting from

Fig. 5.—Pneumoencephalogram of IV 48. The ventricular system is symmetrical though slightly dilated. The subarachnoid space has the usual appearance.

normal instruction. She attended classroom activities for retarded children, but even there she was unsuccessful.

At the age of 10 years 7 months her mental age was 4 years nine months, giving her an I. Q. of 45. She was certified as a mental defective but was not committed to an institution for the mentally retarded because her grandmother (*23*) agreed to take complete supervision of her. According to the grandmother, the girl had a happy disposition but was easily upset and needed constant guidance and vigilance on account of her sexual preoccupation and tendency to exhibitionism. Infrequently she is still enuretic.

She was recently examined at the age of 17 years. Her physical development was good. She was obese and somewhat nervous and had difficulty in understanding what was asked of her. No abnormalities were found on routine physical and neurological examination, apart from poor skill in performing more complicated motor activity. Her pronunciation was slightly indistinct, her vocabulary limited, and she showed little interest in affairs of general life. She scored on the revised Stanford-Binet test an I. Q. of 48. Head measurements: circumference, 53.3 cm.; length, 15.3 cm.; breadth, 12.2 cm.; height, 15.3 cm.; cephalic index, 0.79 cm.

III 44.—Born in 1914. This is the mother of the fourth generation, consisting of three mental defectives. Her parents were respected in the neighborhood and were of good financial and intellectual standing. Her only sibling, a brother, is a successful professional man. According to the grandmother's (*23*) recollection, she was very slow in development and did not learn to speak until about 4 years old. She had to have a private tutor, as she was rejected from public schools on account of her low intelligence. She needed almost constant guidance and supervision and showed excessive sexual activity and lack of good judgment and restraint. She had married against her parents' advice a man also of low intelligence (*43*). The grandmother had to help her with the household, as well as financially.

She was recently examined, at the age of 42 years. Her physical build was normal. Internal organs did not reveal any obvious abnormality. She was very nervous, restless, and somewhat depressed but cooperated satisfactorily during examination. The routine neurological examination was entirely within normal limits. Her pronunciation was fairly good; however, her spelling and simple calculations were deficient, and her vocabulary was limited. She spoke in simple sentences but had little understanding of abstracts, and her judgment was poor. On revised Stanford-Binet test she scored an I. Q. of 59.

Head measurements: circumference 54.8 cm.; length, 18.3 cm.; breadth, 14.1 cm.; height, 13.6 cm.; cephalic index, 0.77 cm.

III 43.—Born in 1912. This is the father of the fourth generation, consisting of three mental defectives. He is one of the fraternal twins and was born first. The intelligence of his dissimilar brother (*42*) is said to be normal.

According to the information obtained from various sources, he was "slow" in development from his earliest years. At the age of 6 years he was rejected from school on account of deficient vocabulary and difficulty in learning. Subsequently, a few other attempts were made to send him to schools in the area, but sooner or later he was dismissed. Finally, the family decided to let him stay at home. He was described as an obedient but easily influenced boy. About the time of puberty he became involved in bad company, contracted gonorrhea, and began to show an interest in alcohol. On account of this, and following psychological examination, which revealed an I. Q. of 50, he was committed to a mental deficiency institution. There, his behavior improved, and he learned some reading. At the age of 18 years he was paroled home, on his mother's request. With the help of his family, he worked intermittently as an unskilled laborer, and at the age of 29 married a 22-year-old feebleminded girl (*44*). Three offspring resulted from this union, all mental defectives (*46, 47, 48*). At the age of 32 he joined the U. S. Navy, served nearly two years, and was finally discharged medically for "nervousness."

When examined in 1955, at the age of 44, he was a somewhat obese, well-developed man. He had numerous complaints regarding his small pension and his arthritis. Physical examination was normal, apart from some osteoarthritic changes in the spine and larger joints. Neurological examination did not reveal any gross abnormality. His speech was distinct but slow, and his vocabulary was limited. He showed little interest in current events, and his attention was mainly centered on himself. Psychological rating on the revised Stanford-Binet test gave him a total I. Q. of 56.

Head measurements: circumference, 56.3 cm.; length, 19.0 cm.; breadth, 15.2 cm.; height, 13.3 cm.; cephalic index, 0.80 cm.

III 33.—Born in 1902. This is the father's (*43*) affected brother. He was reported as being slow in physical and mental development, the retardation being particularly noticeable during his first five years of life. His vocabulary and pronunciation, though not entirely normal, were sufficient for acceptance to a public school. However, he did very poorly scholastically, and his behavior and temper were difficult to control. He worked short periods as a physical laborer but usually gave reason for

quick dismissal from employment. On many occasions he was in conflict with the law for stealing, demolishing without good purpose public and private property, and other similar offenses. He was said to have poor judgment and was easily influenced by bad company. His present whereabouts are unknown, and he could not be contacted for the purpose of examination.

II 23.—Born in 1885. This is the maternal grandmother. She had only one sibling, a brother, who had good intelligence. Her parents were described as normal and capable people. According to many social service reports, she was the only person who took an interest in and actively helped her grandchildren. She was always described as a respectable and clever person, and she still attends her business in renting several houses.

When recently examined, at the age of 71, she was moderately obese, and her blood pressure was elevated to 195/110 mm. Hg. Otherwise, the internal organs were within normal limits for her age. Brief neurological examination did not reveal any obvious abnormality. Her speech was clear and her vocabulary well in average range. She was quick in calculations and showed fairly good knowledge of current events. In fact, she appeared bright for her 71 years. Her head circumference was 55 cm.; length, 18.0 cm.; breadth, 14.2 cm.; height, 13.6 cm.; the cephalic index, 0.78 cm.

Analysis of the Pedigree

Examination of the pedigree reveals that all three children of the fourth generation are mental defectives and that both their parents are similarly affected.

Maternal Line.—The mother had one sibling, a brother, who is a respected professional man. The maternal grandfather (*22*) was a successful business man. He died of cancer, at the age of 40 years. His two siblings (*20, 21*) had normal mentality. The maternal grandmother (*23*) is normal; she was examined and described. Her only brother (*24*), now dead, was of normal intelligence. The maternal great-grandparents (*5, 6, 7, 8*), none living, are said to have been of normal intelligence.

Paternal Line.—The father had 15 full siblings and 3 half-siblings. All three half-siblings (*25, 26, 27*) are married and successful in their careers. They attended public schools, and their intellectual state was normal. Of the 15 full siblings, two sets of twins (*28, 29; 35, 36*) were stillborn or died during the process of birth. Two boys (*30, 31*) died in infancy, of diarrhea and typhoid, respectively. One twin girl (*39*) died at birth; her twin sister (*38*) has normal average intelligence and is still alive. Two other sisters (*32, 41*) completed public school and have normal mentality. One brother (*33*) is mentally deficient and has been described above separately. The remaining four brothers (*34, 37, 40, 42*), one of whom is a fraternal twin (*42*) of the father, are of good intelligence and reached a satisfactory social status.

The paternal grandfather (*11*) was a taxicab driver and was of normal average intelligence. His only brother (*9*) was said to have normal mentality. The paternal grandmother, still alive, is said to be a bright and capable woman. All of her seven siblings (*13-19*) were successfully married and were considered as normal intellectually. The great-grandparents (*1-4*), none living, were described as having had good health and normal mentality.

This survey shows that the father is mentally defective and that one of his 15 siblings, a brother, is similarly affected. Two sets of twins and one girl twin were stillborn or died at birth, and it is unknown what their intellectual capacity could have been. Two brothers died during infancy. Although we cannot be definite about their eventually mental state, the inquiry suggested that their development insofar as acquisition of milestones is concerned was quite normal. The rest of the surviving siblings, including the fraternal twin brother of the father, have normal intelligence.

Comment

Detailed physical, neurological, and psychological examination of children, parents, and maternal grandmother revealed no significant abnormality apart from mental deficiency in parents and children. The intellectual level of the maternal grandmother was normal. The information regarding the mental capacity of the remaining

grandparents, aunts, and uncles was obtained from and double-checked with various members of the family, social agencies, and other sources. Except for one paternal uncle who was mentally defective and delinquent, the intellectual state of all other members shown in the pedigree was normal. Two affected children (*47*, *48*) were admitted to the hospital, and a variety of special tests were performed in an attempt to elucidate further any conceivable clinical or laboratory abnormality. All relevant tests performed proved to be within normal limits, and it was assumed that a genetically determined, as yet unknown, possibly biochemical, disturbance may be responsible.

Delayed and imperfect motor development is quite a common finding in all varieties of mental deficiency. During childhood it may depend on such factors as poor concentration and attention, as well as general difficulty in learning. Also, imperfect function of the higher centers of motor integration may be assumed. In most instances, during later stages of childhood and adolescence the motor skill shows significant improvement.

The anthropometric head measurements were carried out on all members of the family who were examined. There is a notion among anthropologists—which still requires scientific confirmation—that the value of the cephalic index in offspring corresponds closely to that of either parent, even though the length and breadth of the head may differ. If this interesting hypothesis could be proved, the analysis of offspring-parent genetical relationship would be aided. In the family reported here, the cephalic index in two children corresponded closely to that of the father and in one child to that of the mother and maternal grandmother.

The recessive inheritance of milder forms of mental deficiency which is not associated with the presence of abnormal laboratory and clinical findings other than low intelligence was suggested, among others, by twin studies (Juda,[4,5] 1939, 1940) and by studies of consanguineous marriages (Sjögren,[9] 1932; Ruepp, 1935; Penrose,[7] 1938; Duff and Dingee,[2] 1941). These authors, as well as many others (Jervis,[3] 1952; Allen and Kallmann,[1] 1955) believe that different genes in homozygous combination, as well as multifactorial inheritance, may be responsible for mental deficiency in patients of various families. This is also borne out by the fact that there is a tendency in mental defectives of various families to have associated other specific characteristics, such as delinquency, abnormal sexualism, and the like. In this connection, it has to be remembered that the estimation of intellectual capacity by objective psychological tests is a crude and stereotyped method, capable of giving only very general information.

The following is an attempted analysis of possibilities which may result from the assumption that a proportion of mental defects of milder form may be the outcome of abnormality of different single genes in homozygous combination or of abnormal multifactorial inheritance.

1. Each of the affected parents has a different abnormal gene in homozygous condition. Theoretically the offspring should not be affected.

2. Each of the affected parents has the same abnormal gene in homozygous combination. Here we should expect all children to be affected. The reported family seems to fall into this category.

3. One parent is mentally defective as a result of one abnormal gene in homozygous state; the other parent, as a result of abnormal multifactorial inheritance. At present, it is not feasible to analyze such a possibility. A similar situation may be encountered in an instance in which both parents are defective as a result of multifactorial inheritance.

Dominant and sex-linked inheritance of the form of mental deficiency discussed is theoretically possible. However, in order not to enlarge the scope of this communication, this aspect will not be considered here, inasmuch as the reported family

would not fall into this group. It can be said only that certain investigators doubt dominant and sex-linked inheritance of undifferentiated forms of mental deficiency. If it does occur, it is probably rare.

If we return now to the family reported here, it will be seen that the paternal grandparents and great-grandparents were normal but one of the father's many siblings was also mentally deficient. On the maternal side, the grandparents and great-grandparents were all normal, and the mother's only sibling was a successful professional man. It appears from these data that mental deficiency in each parent must have been of recessive occurrence in homozygous combination, since all their three children were similarly affected. There was no possibility of reliably tracing ancestors beyond the great-great-grandparents, and consequently consanguinity in prior generations cannot be entirely excluded. Expressedly, if this inheritance is recessive—and all available data suggest that it is—the abnormal trait in both parents must be the same. This would imply that the recessive gene in question is quite common in the population concerned. However, an important factor in the marriage of the parents (*43, 44*) might have been that, being mentally deficient, they were both limited in finding a mate of normal intelligence.

Mutation of a dominant trait responsible for the mother's mental deficiency is a very unlikely theoretical possibility. In an instance of multifactorial inheritance one would not expect to find all three children affected, with a striking similarity of the psychological and intellectual picture. However, such occurrence, though unlikely, cannot be entirely excluded.

As the instance of this family shows, a considerable knowledge regarding inheritance of undifferentiated types of mental deficiency could be obtained from accumulation of data derived from careful studies of offspring, ancestors, and relatives of both affected parents. Although the demonstration that a proportion of mentally deficient patients of the undifferentiated group have a hereditary basis does not in itself tell us much regarding the basic abnormality and mechanism of the production, it may indicate the direction for future research. In general, most of the inherited abnormalities are initiated by metabolic derangement of some kind, at some stage of the prenatal or postnatal life. Even clear demonstration that certain instances are a result of a multifactorial type of inheritance, whereas others are of the autosomal recessive type, may be helpful.

The influence of environmental factors in modifying genetical expression of any trait is well known and needs not to be discussed here at length. Certain physical handicaps, deprivation of special senses, and lack of appropriate intellectual stimulation are all in themselves factors contributing to the mental deficiency.

Eugenic aspects of marriages between two persons with genetically determined mental defects are obvious enough and will not be further discussed. In dealing with children of low intellectual capacity, the parents, guardians, and teachers should be careful not to force them to reach attainments beyond their possibility. Such an attitude may actually make the situation worse by increasing nervousness and producing anxiety. Longer observation of these children in different situations and at various tasks may reveal a particular kind of interest or ability, which could be then encouraged and further developed.

Summary

Present-day classification of mental deficiency is briefly discussed. The description of an interesting family is given in which both parents and their three children are mental defectives of an undifferentiated type. Paternal and maternal grandparents were of normal intelligence, but one of the paternal siblings was also a mental defective. Comprehensive clinical investigation, as well as biochemical, serological, and other special testing, does not reveal any evidence

of a gross developmental anomaly, infection, known metabolic disorder, or destructive lesion of the central nervous system in the patients studied. Analysis of the pedigree of this family is compatible with autosomal recessive inheritance of an abnormal trait in a homozygous combination.

It is suggested that the accumulation of pedigrees of a similar nature, when both parents are affected, may be found fruitful in investigation of the undifferentiated mental deficiency of various types.

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Diagnosis of Cerebral Schistosomiasis

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Cerebral schistosomiasis may produce a variety of neurological symptoms. Among the commoner neurological manifestations are headache, language dysfunction, paralysis, and Jacksonian [1] or grand mal seizures.[2] Therefore, a patient presenting such symptoms who has resided in an endemic area, even years before, should be evaluated for possible cerebral schistosomiasis. Usually the diagnosis of cerebral involvement by this disease has been made when a cerebral granuloma with characteristic ova was unexpectedly discovered during a craniotomy.[3]

The search for ova in the feces is a difficult and time-consuming procedure. Consequently, other, more easily applied methods of diagnosis have been sought. In 1943 Ottolina and Atencio [4] reported on the value of rectal mucosa biopsy in the diagnosis of schistosomiasis mansoni. Zieve and Conley [5] later demonstrated that the procedure was applicable to the diagnosis of schistosomiasis japonica. Since then the technique has been described in several other reports in the English literature applied to infection with schistosoma mansoni,[6-15] S. haematobium,[10,15] and S. japonicum.[16]

It is the purpose of this report to demonstrate the efficiency of rectal biopsy in the diagnosis of schistosomiasis and to emphasize its usefulness in patients with neurological symptoms and signs who have been residents of an endemic area.

Clinical Information

The patients to be reported on were hospitalized at the Minneapolis and Oklahoma City Veterans' Administration Hospitals. All had schistosomiasis japonica. Case 1 was the subject of a previous report.[5] The clinical data in all subjects are recorded in Table 1. All had been in the Army in the Philippine Islands. The duration after exposure to the time of diagnosis was 3 to 10 years. Only two had a definite history of acute schistosomiasis while in the endemic area. Four presented with seizures; two, with focal seizures alone; one, with generalized grand mal and focal seizures, and one, with psychomotor attacks. Although four patients had headaches, it would be difficult to attribute this to the disease. Four patients had gastrointestinal symptoms which may have been due to the disease. Only three patients had hepatomegaly, and two had splenomegaly. Liver function tests were definitely abnormal in only two patients. Most of the patients showed eosinophilia from time to time. Of the patients with seizures, two (Subjects 22 and 12) had no abnormal findings on neurological examination. Case 3 showed paresis and hyperactive reflexes of the left arm, and Case 8 had a left homonymous hemianopsia.

The spinal fluid examinations in the four patients with seizures was of interest. Case 2 showed 87 mg. of protein per 100 cc., but was otherwise normal. Case 3 had a normal spinal fluid examination, but had been treated for syphilis because of a positive Wassermann reaction in the spinal fluid. Case 8 had a positive spinal fluid Wassermann reaction, but the fluid was otherwise negative. He had a negative blood serological test for syphilis. Neither of these two patients had a history consistent with syphilis. Case 12 had a normal cerebrospinal fluid.

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TABLE 1.—*Clinical Data on Twelve Patients with Schistosomiasis Japonica*

No.	Age, Yr.	Area of Exposure	Years from Exposure to Diagnosis of Chronic Schistosomiasis	History of Acute Schistosomiasis	Symptoms	Neurological Examination	Palpable Liver	Palpable Spleen	Sulfobromophthalein (Bromsulphalein) Retention	Cephalin Flocculation	Highest Eosinophil Per Cent	Other Ova
1	29	Leyte, P. I.	3	0	Weakness, weight loss, diarrhea, pain RUQ	0	+	+	4.5	3+, 4+	20	Trichuris
2	28	Leyte, P. I.	4	0	Grand mal and Jacksonian seizures	0	0	0	Not done	Not done	6	0
3	35	P. I.	5	0	Jacksonian seizures	+ (see text)	0	0	16.6	0,0	22	0
4	31	P. I.	5	0	Headache	0	0	0	4.0	0,0	24	0
5	31	Leyte, P. I.	6	Yes	Abdominal pain and headache	0	0	0	2.0	0,0	8	E. histolytica
6	32	Mindanao, P. I.	5	0	Weakness and headache	0	0	0	1.4	0,0	9	0
7	32	Leyte, P. I.	5	0	Abdominal cramps	0	+	0	2.0	0,0	21	0
8	27	Mindanao, P. I.	3	0	Jacksonian seizures	+ (see text)	0	0	8.5	Not done	6	0
9	33	Mindanao, P. I.	6	0	Diarrhea	0	0	0	3.5	Not done	4	0
10	32	Mindanao, P. I.	6	0	Headache	0	0	0	2.0	0,0	16	0
11	30	Mindanao, P. I.	6	0	None	0	+	0	4.0	0,0	12	0
12	31	Leyte, P. I.	10	Yes	Psychomotor seizures	0	0	0	0	0,0	12	0

The skull x-rays in the patients with seizures were all negative. All the patients with seizures had a localized cerebral dysrhythmia, demonstrated by electroencephalography. Pneumoencephalographic studies were normal in Cases 3 and 12 and were not performed in the other patients. Three of the patients with seizures had a schistosomal cerebral granuloma removed at craniotomy, and the fourth subject has not come to operation.*

The information relative to establishing the diagnosis is given in Table 2. The stool examinations were performed by several techniques designed to demonstrate Schistosoma ova.[17] Only two patients had ova discovered by the hospital laboratory. In two other patients ova were found in the stools by Dr. Harry Most. This finding indicates that the percentage of recovery from the stools would probably be higher in a laboratory devoted to this problem.

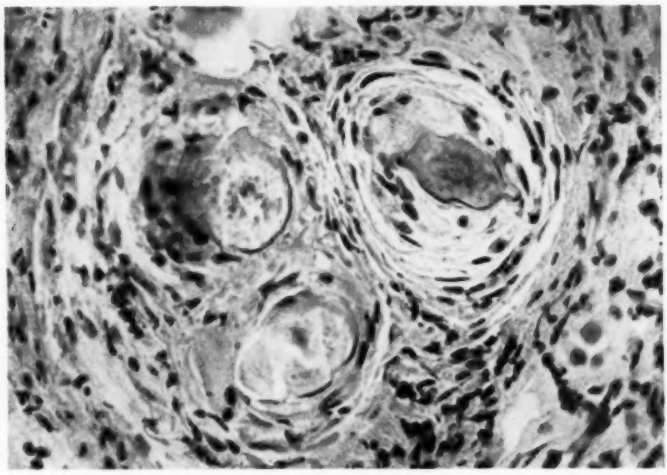
Proctoscopic examinations in all subjects were normal. Despite this negative finding, biopsy of the rectal mucosa was positive for Schistosoma ova in 92% of the cases. The accompanying figure is illustrative of a typical finding in a positive rectal biopsy. Four liver biopsies were performed in this group of patients, and only one was positive. Three patients had the diagnosis of schistosomiasis first established at craniotomy,

* Case 12 has since had a craniotomy. A right temporal lobe granuloma was excised. The lesion showed many ova of S. japonicum.

TABLE 2.—*Establishment of Diagnosis of Schistosomiasis*

No.	Stools for Schistosomiasis		Rectal Biopsy	Liver Biopsy	Method by Which Diagnosis First Established
	No. Examined	No. Positive			
1	55	0	+	Negative	Rectal biopsy
2	4	0	Negative	Not done	Craniotomy
3	7	0	+	Not done	Craniotomy
4	3	0	+	Not done	Rectal biopsy
5	8	0	+	Not done	Rectal biopsy
6	10	0	+	Not done	Stool *
7	8	0	+	Not done	Appendectomy
8	3	0	+	Not done	Craniotomy
9	13	0	+	Not done	Stool *
10	16	2	+	Negative	Stool *
11	17	3	+	Positive	Stool *
12	3	0	+	Negative	Rectal biopsy

* Stool examined in Dr. Harry Most's laboratory (New York University) as a part of a survey.



Rectal biopsy specimen with Schistosoma japonicum ova.

and one, when the ova were found in a surgically removed appendix. In only one of these patients did subsequent rectal biopsy fail to demonstrate the ova of schistosomiasis.

Comment

Schistosomiasis may involve the cerebrum. When this occurs, a variety of neurological symptoms may appear, but convulsions are the commonest. When the diagnosis of schistosomiasis is established, treatment with antimony potassium tartrate U. S. P. is in order if viable ova can be demonstrated.[18] Such treatment is important to prevent further development of distant involvement by ova, as well as to rid the host of the flukes. The treatment for local cerebral involvement is surgical excision. Convulsions may persist after surgery and require appropriate medication.

The diagnosis of cerebral schistosomiasis should be suspected in a patient with neurological symptoms who has resided in an endemic area. Another clue may be the presence of eosinophilia. Electroencephalograms were useful in suggesting a focal lesion, but pneumoencephalography in two patients was not helpful. It is possible that two of the patients in this series had false-positive Wassermann reactions in the cerebrospinal fluid. A previous paper has commented on this occurrence.[19] In contrast to long-term residents of endemic areas, short-term residents infrequently show hepatomegaly and splenomegaly, and liver function tests are usually normal. The lack of significant liver involvement is also confirmed by the negative liver biopsies in three of four patients examined by this procedure. Examination of the stools for ova was only occasionally fruitful. The most useful diagnostic procedure was a rectal biopsy, which yielded postive results in all but one of the patients reported here. The efficiency of the rectal biopsy in the diagnosis of schistosomiasis japonica in this report is comparable to a previously reported series, which showed 30 positive biopsies, with only 27% demonstrating ova in the stools.[16] While various techniques have been described, the three usually used are fixation in formalin and staining with hematoxylin and eosin, examination of unstained material after digestion with 4% potassium hydroxide, and examination without staining after adding a drop of water and compressing between two glass slides.[8] The examination of fresh specimens permits the recognition of living ova, since these will appear golden-yellow, in contrast to the brown to black appearance of dead ova. The chief advantage of the stained preparation is that the slides may be examined leisurely and

many sections studied. The biopsy specimen may be obtained from any of the valves of Houston, but some advocate the middle valve in preference to the lower. Rectal biopsy is the simplest and most accurate diagnostic procedure for schistosomiasis. Ova may be found even when the mucosa appears grossly normal, although the mucosa may show a granular appearance. The recognition of the ova is simple even for the novice.

Summary

Four of twelve patients with chronic schistosomiasis japonica had seizures. Three of the twelve had the diagnosis first established by a craniotomy. Eosinophilia was usually present. Hepatomegaly, splenomegaly, and abnormal liver function tests were infrequent. A positive Wassermann reaction in the spinal fluid with a negative blood Wassermann reaction was present in two patients. Stool examinations were positive in only 2 of the 12 patients, despite numerous studies. In contrast, the rectal biopsy was positive in all but one.

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Use of Parenteral Diphenylhydantoin (Dilantin) Sodium in Control of Status Epilepticus

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Introduction

The parenteral use of diphenylhydantoin (Dilantin) sodium in the control of seizures was first described by Murphy and Schwab,[1] of the Massachusetts General Hospital, in 1956. They reported on the use of 9710 doses over a period of five years, most of which was used to prevent seizures during neurosurgery. Some was used, however, in the treatment of status epilepticus. They pointed out the danger of using phenobarbital sodium intravenously or intramuscularly to suppress convulsions because of its severe depressant effect on respiration. Patients undergoing brain surgery are very sensitive to sedatives, even in small doses. Diphenylhydantoin, on the other hand, has the advantage that it does not depress respiration or act as an anesthetic. They reported that in severe status epilepticus an intravenous dose of 150 to 250 mg. of diphenylhydantoin sodium was usually given, and if the seizure did not stop, a subsequent dose of 100 to 150 mg. was given a half-hour later.

Material and Methods

We see, at the Florida Farm Colony, a large number of patients in status epilepticus who have not been previously treated with barbiturates or other drugs for such episodes. They are at this time on their regular epilepsy medication. This study concerns 71 attacks in 42 patients. Six of these patients were over 21 years of age, and four were 5 years old or less. The remainder were between 5 and 21. There were 22 male and 20 female patients.

Parenteral diphenylhydantoin sodium is made up by adding the 5 cc. of solvent to the diphenylhydantoin sodium in the Steri-Vial and shaking gently. The contents of the Steri-Vial dissolve slowly over a period of about 10 minutes. This process can be speeded by immersing the Steri-Vial in warm water after adding the solvent. The resultant solution contains 50 mg. of diphenylhydantoin sodium per cubic centimeter, or 250 mg. in the ampule. It must be used within a few hours of preparation, and only a clear solution should be used.

In the treatment of status epilepticus the diphenylhydantoin sodium is injected intravenously at a rate not exceeding 1 cc. of solution per minute. A dose of 250 mg. was found to control most episodes of status epilepticus, but in some cases a further injection was given later. Following the return of the patient to consciousness, diphenylhydantoin or other therapy was continued by mouth. Occasionally, it was necessary to give a Dilantin sodium Steri-Vial injection (250 mg. of diphenylhydantoin sodium) intramuscularly for two or three days at four- to six-hour intervals to maintain control.

Results

Of 121 episodes of status epilepticus in 85 patients, 97 were controlled by one injection of Dilantin sodium Steri-Vial (250 mg. diphenylhydantoin sodium). Seventeen episodes of the remaining twenty-four were controlled by a second dose, and seven episodes in five patients required a barbiturate or other medication in addition to control the seizure. Three of the seven episodes not responding to diphenylhydantoin sodium alone were in one patient. These five pa-

Control of Status Epilepticus by Diphenylhydantoin Sodium

No. of episodes of status epilepticus	121 (85 patients)
Episodes controlled by one injection	97 (66 patients)
Episodes controlled by two injections	17 (14 patients)
Episodes controlled by dilantin S. V. and barbiturate injections	7 (5 patients)

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From the Florida Farm Colony.

tients were controlled by diphenylhydantoin sodium, 250 mg., given intramuscularly for two or three days at six-hour intervals.

Side-Effects

No sedative or other side-effects were noted in this series of patients. Patients receiving multiple doses showed no staggering gait or other disturbance of balance. It is remarkable that in the whole series none showed depression of respiration.

Summary

Diphenylhydantoin (Dilantin) sodium was found to be a useful substance for the control of status epilepticus when given intravenously. No side-effects were noted following its parenteral use.

Florida Farm Colony.

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Subarachnoid Hemorrhage with Papilledema Due to Spinal Neurofibroma

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The occurrence of spontaneous subarachnoid hemorrhage always raises urgent diagnostic and therapeutic problems. The early determination of the cause of hemorrhage is of great importance; and if no localizing signs are found, cerebral arteriography is usually performed on one or both sides. If papilledema is present in the bleeding patient, the presence of an intracranial space-occupying lesion is usually suspected.

Subarachnoid hemorrhage, however, may also be of spinal origin, usually from a spinal vascular anomaly [1] or a spinal tumor.[2] This condition seems to be rare, and only a small number of cases have been reported in the literature. In a series of 312 consecutive cases of spontaneous subarachnoid hemorrhage, only 2 such instances were recorded.[3]

A case is here reported of repeated subarachnoid hemorrhages and papilledema due to a spinal neurofibroma.

Report of a Case

A woman, aged 49, was admitted to the Department of Neurology because of attacks of paroxysmal pain in her back and papilledema. Her personal and family histories were noncontributory.

One year prior to admission she became acutely ill with low-back pain, which radiated down to her buttocks and upward along the spine. The pain was aggravated by moving and coughing. She began to suffer from severe headaches and stiffness of the neck 10 days later. During the following months she experienced sharp pain in the lower back occasionally, and her headaches were accompanied by transient diplopia. Four months before admission she had another episode of low-back pain. Ten weeks after this episode she was admitted to another hospital because of a similar attack, followed by severe headaches.

The neurologic examination at that time showed no abnormalities. The blood pressure was 160/110; the eyegrounds revealed slight hypertensive changes, and papilledema was more marked in the left eye, with hemorrhages on that side. Lumbar puncture yielded xanthochromic fluid under a pressure of 300 mm. of water. In the sediment crenated erythrocytes were found. The patient was then transferred to the Department of Neurology for further investigation.

On admission, she was in good general condition and was cooperative. She complained of pain in the lumbar region, and there was generalized tenderness of the spine. Neurologic examination was negative except for choked disks and a positive Kernig's sign. Visual acuity was 5/5 in each eye. The visual fields were normal, and it was felt that the papilledema was probably due to an intracranial space-occupying lesion. A systolic murmur was heard over the aortic valve. Her blood pressure fluctuated between 170/100 and 130/80. The electrocardiogram was normal, and chest x-rays showed slight dilatation of the left ventricle. X-rays of the skull were normal. Because of the fluctuating hypertension, an intravenous pyelogram was obtained and was found to be normal. Urinalysis and blood chemistry were normal. The erythrocyte sedimentation rate was 8 mm. in 30 minutes; the red blood count 4,510,000; the hemoglobin 13.2 gm. per 100 cc., and the white blood count 11,300 per cubic millimeter.

An electroencephalogram was normal. Lumbar puncture revealed slightly xanthochromic fluid under a pressure of 190 mm. of water, which contained 60 mg. of protein and 77 mg. of glucose per 100 cc. and 10 white cells per cubic millimeter. The Wassermann reactions of the blood and the CSF were negative.

She was discharged without a definite diagnosis and was readmitted to the Department of Neurology seven months later. During that period her condition had been satisfactory. A week before admission, however, while lying in bed, she again suddenly experienced a strong, sharp pain in the lower part of her back, radiating into her legs. Two days later she felt that the pain was radiating along the spine "as if entering her neck and head."

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From the Departments of Nervous Diseases and Neurosurgery, Rothschild - Hadassah - University Hospital.

Fig. 1.—Myelogram, showing filling defect at the upper border of L-2, suggesting intradural tumor.

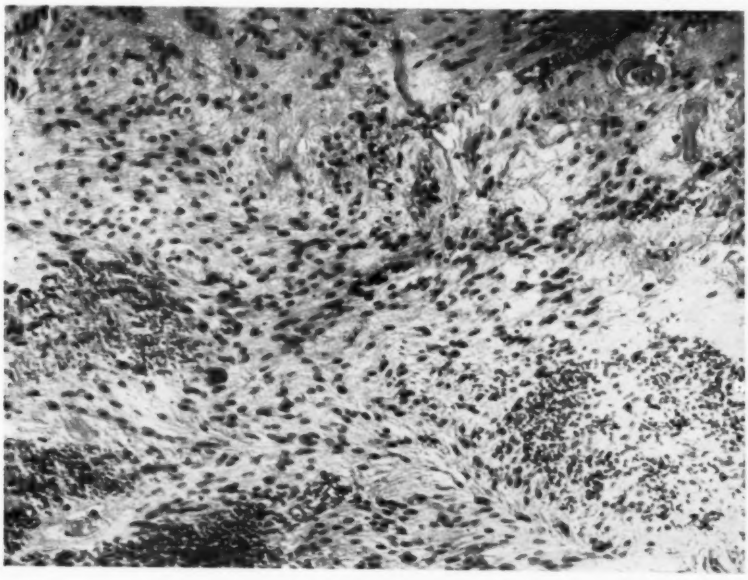
The headaches and the neck pain increased during the following days, and she also complained of vertigo and blurring of vision. Examination revealed marked neck rigidity and a positive Kernig's sign. Papilledema of 2 D. in the right eye and 3 D. in the left eye, with venous congestion and

Fig. 2.—Macroscopic appearance of the massively infarcted neurofibroma.

hemorrhages, was found. There were no other neurologic disturbances. A lumbar puncture yielded bloody fluid (188,000 erythrocytes per cubic millimeter) under a pressure of 220 mm., which contained 190 mg. of protein per 100 cc. A repeated lumbar puncture five days later revealed a pressure of 330 mm. While she was in the hospital, her condition gradually improved, and signs of meningeal irritation and her headaches subsided. Ten days later, however, she had another episode of subarachnoid bleeding. The fact that the patient emphasized that each attack started with a sharp pain localized in the small of her back, the headaches following a few days later, brought up for consideration the possibility of spinal recurrent bleeding, and iophendylate (Pantopaque) myelography was performed. A filling defect was discovered at the upper border of the second lumbar vertebra, suggesting an intradural tumor (Fig. 1).

The patient was transferred to the Department of Neurosurgery for operation. On laminectomy (L-1 to L-3) a 1.5×2.5 cm. intradural mass

Fig. 3.—Microscopic appearance of the neurofibroma with recent hemorrhagic infarctions.



was found lying on the right, close to the midline, and ventral to the roots of the cauda equina. Its color was bluish-black, and it was attached to one of the roots, which entered at its upper pole and emerged from its lower end. The root was severed between silver clips on both sides of the mass, and the tumor was easily delivered from its bed. It had the macroscopic appearance of an infarcted neurofibroma (Fig. 2). Histologic examination confirmed the diagnosis of neurofibroma with old hemorrhages and a fresh hemorrhagic infarct (Fig. 3). The postoperative course was uneventful, and the patient left the hospital in excellent condition 12 days after the operation. A follow-up two months later was entirely negative.

Comment

The differentiation of cerebral and spinal subarachnoid hemorrhages is difficult, but there are a number of symptoms which should indicate that the bleeding is of the latter type. Spinal subarachnoid hemorrhage usually begins with severe, sharp pain at the site of the hemorrhage, *le coup de poignard rachidien* of the French authors,[4] radiating down the legs and spreading along the spine. The presence of neurologic signs referable to the spinal cord depends on the nature, size, and localization of the lesion. After the entry of blood into the subarachnoid space, meningeal signs develop. The entry of blood into the cranial cavity, after several hours, or even a number of days, may cause headaches, vomiting, photophobia, disturbances of consciousness, convulsion, and cranial nerve involvement, all pointing toward an intracranial lesion.[1,3]

Krayenbühl [5] described two cases of intradural neurofibroma, one tumor being located in the region of the cauda equina and the other at the T-12 level. Both patients gave a history of prolonged radicular pain without acute episodes, suggesting previous attacks of subarachnoid hemorrhage. Both became paraplegic within a matter of minutes, owing to massive hemorrhage into the tumor and the subarachnoid space. The tumor was removed in both cases; only one patient recovered slowly from his paraplegia. Fincher [2] reviewed two previously published reports of spinal subarachnoid hemorrhage due to cauda equina ependymomas and added two cases. A third case, of a neurofibroma of unusual vascularity, had four attacks of subarachnoid hemorrhage over a period of four years. In four of the patients the CSF pressure was elevated, with no signs of spinal block. In one of his cases of ependymoma there was also choking of the optic nerve heads. In only two cases were there signs of spinal cord involvement, and definitive diagnosis in his cases could only be established with the aid of myelography. Henson and Croft [1] recently reviewed the literature on spontaneous spinal subarachnoid hemorrhage and added seven cases of their own. Two were due to spinal angioma; one had an aneurysm of the posterior spinal artery; three probably had angiomas, and one had polyarteritis nodosa. There were no cases of spinal cord tumors in their series. Two of their patients had papilledema and were mentally confused. One of them had cranial nerve palsies, and the other had convulsions and pyramidal tract signs.

The difficulty in establishing a correct diagnosis in our case, as well as in a number of other reported cases, was caused by cerebral symptoms. The absence of signs of spinal cord involvement, the increased intracranial pressure, and papilledema, as well as the double vision, appeared to be indicative of an intracranial origin of the subarachnoid bleeding. Irritation of lower spinal nerve roots following subarachnoid hemorrhage can be observed in almost every case. In the subarachnoid bleeding due to a spinal lesion, however, the low-back pain is usually excruciating and precedes the appearance of the other signs, as observed in our case.

The commonest cause of spinal subarachnoid hemorrhage is a spinal angioma.[1] It has also been reported in a number of spinal tumors, mainly ependymomas, and in three neurofibromas.[2,5] Hemorrhage was the first indication of the presence of a spinal tumor in three cases. The hemorrhage in ependymomas can be attributed to their vas-

cularity,[2,6] and in our patient, to the hemorrhage and infarct within the neurofibroma. It also may be related to the fluctuations in the patient's blood pressure. Douglas-Wilson et al.[7] reported a patient with hypertension and spinal subarachnoid hemorrhage of undetermined origin. They noted the close association of the fall of the blood pressure with improvement in their patient's clinical condition.

It is known that papilledema is not necessarily indicative of a cerebral lesion. Increased intracranial pressure has also been reported in patients with cauda equina ependymomas, without subarachnoid hemorrhage, though the spinal fluid protein was increased.[8-10] Papilledema is also known to occur in polyradiculoneuritis associated with a high CSF protein.[11] The elevated protein and, consequently, the increased viscosity of the CSF in these cases cause diminished absorption of cerebrospinal fluid.[12] This factor, as well as the mechanical clogging by the protein molecules of the pores of the semipermeable membrane which constitutes the brain-blood barrier, is responsible for the increased intracranial pressure.[10] Likewise, in subarachnoid hemorrhage the presence of fibrin will further interfere with CSF absorption. The secondary adhesions following repeated subarachnoid hemorrhages, which may be responsible for cranial nerve involvement, will reduce the CSF absorption rate as well and may cause ventricular dilatation.[1,6]

Summary

Spinal subarachnoid hemorrhage is rare. The fourth case of spinal neurofibroma causing subarachnoid hemorrhage is reported. There were no local signs referable to the tumor, but increased intracranial pressure and papilledema were present. The symptomatology of spinal subarachnoid hemorrhage is described. It is emphasized that, in spite of absence of signs indicating a spinal cord lesion and though evidence of cerebral involvement may be present, attention should be focused on the possible spinal origin of the bleeding if sharp pain in the back is the presenting symptom. Early myelography may help to establish the correct diagnosis, and thus prevent further damage to the spinal cord and the serious and permanent cerebral complications which may follow repeated subarachnoid hemorrhage. The mechanism of increased intracranial pressure in spinal cord tumors and subarachnoid hemorrhage is discussed.

Dr. A. J. Behar, of the Department of Pathology, made the pathological examination of the tumor.

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Electromyography in Herniated Lumbar Disks

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The value of electromyography in the localization of lower motor neuron lesions has been well demonstrated.[7,8,17] However, there has been very little written about its usefulness in protruded lumbar disk suspects. The most widely used test in the localization of protruded lumbar disks is oil myelography. A number of large series of cases of myelography in surgically verified protruded lumbar disks show the accuracy of the method to be 70% to 90%.[4,5,11,15] This leaves a group of 10% to 30% of patients with surgically verified protruded lumbar disks which are not localized by myelography. While diskography is being used in this group,[2,6,12,13] there are those who object to its use, mainly on the basis of possible damage to a normal disk. In addition, some surgeons prefer not to introduce a foreign substance into the subarachnoid space, and so attempt to localize the protrusion on the basis of clinical findings, avoiding myelography. Electromyelography avoids the possible disadvantages of damage to a normal disk and of the introduction of a foreign substance into the subarachnoid space. Neurosurgeons who use myelography in the localization of herniated lumbar disks would be aided by a test which would accurately localize the protrusion in the group of patients who have herniated lumbar disks that are not localized by myelography. For these reasons it was decided to evaluate electromyography as a practical clinical aid in the localization of herniated lumbar disks. Therefore, the records of 45 consecutive patients who had electromyography, iophendylate (Pantopaque) myelography, and surgically verified protruded lumbar disks were reviewed.

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Selection of Cases

The usual indications for surgery in cases of protruded lumbar disk were used in selecting patients for investigation and surgery. Patients with their first or second attack of back and leg pain were not operated on unless conservative measures failed to give relief. Patients having their third or more recurrence of symptoms were still not investigated myelographically or myographically unless the symptoms were incapacitating.

No patient was investigated during remission. Not included in this series were patients who had had previous disk surgery with recurrence of pain. These cases were eliminated because of the possibility of their still having positive electromyographic findings from previous root compression and of the possibility of having postoperative myelographic defects, both of which could confuse the evaluation in this investigation.

Myelography

Myelography was done from one to seven days prior to surgery. Iophendylate was used in all cases. Routinely, 6 cc. of iophendylate was injected via an 18-gauge needle at the second or third lumbar interspace.

Fluoroscopy was followed by the taking of multiple spot films in the anteroposterior, across-the-table-lateral, and oblique positions. For the purpose of this study, the report rendered by our radiologists was accepted in an attempt to keep this examination objective, since the radiologists had no knowledge of the electromyography report.

Minimal defects, such as absence of filling of a nerve root sheath or asymmetry of the axillary pouches, were reported as positive findings.

Electromyography

Electromyography in all cases was done from 2 to 10 days prior to surgery and from 1 to 7 days prior to myelography.

All electromyography was done and interpreted by one of us (A. S.), the only information avail-

able being that the patients were protruded lumbar disk suspects.

The Meditron Clinical electromyograph, Model 201A, which utilizes a monopolar needle electrode, a cathode-ray oscilloscope, a sensitive sound amplifier, and a myoscope, was used in all cases.[19]

Denervation fibrillation,[8] polyphasic motor unit potentials,[18] and positive waves[9] were interpreted as indicating nerve root involvement. The deductive method was used in localizing the root involved. While all muscles tested have multiple root innervation, only those muscles which have the involved nerve root in common should show denervation fibrillation, polyphasic potentials, and positive waves. For example, with S1 root involvement, samplings of the vastus lateralis (L2-L4), tibialis anterior, and extensor hallucis longus (L4-L5) would be normal, whereas samplings from the peroneus longus (L5-S1), and especially the medial head of the gastrocnemius and soleus (S1-S2), would show evidence of denervation. Corroboration is often obtained by finding denervation in the multifidus, which is supplied segmentally by the posterior divisions of the lumbar and sacral nerve roots. The average time for this type of examination is 40 minutes.

One obvious source of error in using the deductive technique is the variation of nerve supply to the tested muscles and the variation which occurs in the formation of the lumbar and sacral plexuses. Another source of error in localizing lumbar disk protrusion by means of the root involved is that a wide protrusion may compress two nerve roots and that a more lateral or more medial herniation may compress the nerve root above or below the usual root of the involved disk.[10]

Electromyography and Myelography Findings

Of the 45 cases, the protruded disk was found at the lumbosacral interspace in 23 cases and at the fourth lumbar interspace in 22 cases. Table 1 is a presentation of the results in terms of localization.

Of the three cases (7%) of incorrect localization with electromyography, two were read as L4-L5 protrusions and the disk was at the lumbosacral interspace, and one was read as a lumbosacral protrusion and the disk was at the fourth lumbar interspace.

Of the four cases (9%) in which the disk was incorrectly localized with myelography, three represented nerve-root cutoffs at the fourth lumbar interspace with the actual protrusion at the lumbosacral, and one was a needle defect read as an L3-L4 protrusion, with the actual protrusion at L4-L5.

TABLE 1.—*Electromyography and Myelography Findings*

Cases (45)	Positive (Correct)		Incorrect		Negative (Normal)	
Electromyography	40	(89%)	3	(7%)	2	(4%)
Myelography	38	(84%)	4	(9%)	3	(7%)

Comment

Since other investigators are using electromyography as an aid in localization of protruded lumbar disks,[1,16,17,19] it is important to list the number of cases in which objective evidence was demonstrated of nerve root compression other than pain and its manifestations, such as reflex change, weakness, or sensory deficit. This is done as a rough guide in comparing results in different series, since some other operators will have fewer patients and some more patients with objective neurologic deficits, varying with the type of patient dealt with and with the operator's own indication for disk surgery. Table 2 is a tabulation of the neurologic changes found in these 45 cases. Most patients had more than one of the above-mentioned neurologic changes present. Of the entire group, five L4-L5 disk patients and two lumbosacral disk patients had none of the above-noted demonstrable changes. Therefore, of the 45 cases, 38 (84%) had objective evidence of root compression other than pain and its manifestations.

Of the seven cases in which myelography did not accurately localize the protrusion, that is, three with normal and four with incorrect localizing myelograms, all had one or more of the neurologic changes of dimin-

TABLE 2.—*Neurologic Changes in Forty-Five Cases of Herniated Lumbar Disk*

Protruded Disk	Achilles Reflex Diminished to Absent		Sensory Deficit		Weakness	
L4-L5 (22 cases)	4	(18%)	10	(45%)	12	(55%)
L5-S1 (23 cases)	10	(43%)	19	(83%)	8	(35%)
Total (45 cases)	14	(31%)	29	(64%)	20	(44%)

ished Achilles reflex, sensory deficit, or weakness. The three cases in which the protrusion was incorrectly localized with electromyography likewise all had one or more of the neurologic changes.

Interestingly enough, the two cases which had normal electromyograms showed no neurologic change. No conclusion can be drawn from this finding, but one might speculate that motor fibers had not been damaged by the time electromyography was performed, rather than that these two cases represent technical error or reflect on the sensitivity of electromyography in the presence of lower motor neuron damage.

None of the four cases with incorrectly localizing myelograms had incorrectly localizing or normal electromyograms. The same is true for the three cases with normal myelograms. None of the five cases with incorrectly localized or normal electromyograms had incorrectly localized or normal myelograms.

Conclusions

Eighty-nine per cent, or 40, of 45 surgically verified cases of protruded lumbar disks had accurately localizing electromyograms. The three cases in which electromyography was incorrectly localizing can be explained on the basis of technical error or of the known variation in the formation of the sacral plexus. In the two cases in which electromyography was normal, it is suspected that the basis was the absence of motor nerve fiber damage, rather than technical error, since neither of these two patients had demonstrable neurologic changes other than manifestations of pain.

It would appear that institutions which have an experienced electromyographer might benefit by the use of this test in localizing lumbar disk protrusions. This is especially true in the group of 10% to 30% of patients with surgically verified protruded lumbar disks which are not localized by myelography, and also for those physicians who prefer to avoid myelography or for those who might use both myelography and electromyography in selected cases.

Since electromyographic findings are admissible as evidence in courts of certain states, and will probably be recognized by more states with time, this test finds application in medicolegal problems. Likewise, those patients who are required by industrial commissions or insurance companies to have myelography before settlement or surgery might have electromyography performed and used as objective evidence.[14]

While no patient in this series had both a normal or an incorrectly localizing myelogram and a normal or an incorrectly localizing electromyogram, the likelihood of this occurrence in a larger series is great. However, since myelography and electromyography are each 80% or more localizing in cases of lumbar disks, the incidence of their both being incorrectly localizing or normal should be small. The use of electromyography with myelography, at least in the group of clinically suspected protruded lumbar disks with normal myelograms, should materially aid in the localization of the protruded disk.

Summary

Forty-five consecutive cases of surgically verified protruded lumbar disks were studied preoperatively with iophendylate (Pantopaque) myelography and electromyography. Forty cases had accurately localizing electromyograms. Thirty-eight cases had accurately localizing myelograms. Eighty-four per cent, or 38 cases, had objective evidence of nerve root compression other than pain or its manifestations.

It is inferred that electromyography is of clinical value in the localization of protruded lumbar disks.

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Hyperextension Injuries of the Cervical Spine

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The somewhat unusual, but by no means rare, occurrence of a severe injury to the cervical spinal cord without roentgenographic evidence of recent trauma to the cervical spine has perplexed physicians for many years. The common explanation that there had been a dislocation of the body of one vertebra on another with subsequent spontaneous reduction, although generally accepted, was not entirely satisfactory. The fact that the usual postmorten examination does not include examination of the spinal cord, much less the bony cervical spine, does not contribute to a better understanding of the problem.

The publications of Taylor and Blackwood in 1948,[1] Barnes in 1948,[2] and Taylor in 1951[3] lead to at least a partial, and certainly a plausible, solution of the question. They demonstrated in clinical case reports and in postmortem studies that extreme hyperextension of the cervical spine, particularly of a cervical spine already affected by degenerative arthritis, may produce actual contusion and laceration of the spinal cord. Their roentgenograms of cadavers during cervical hyperextension illustrate well that the ventral surfaces of the laminae, and probably also the ligamentum flavum, compress the spinal cord from the dorsal surface, while the bony spurs on the dorsal surface of the vertebral bodies compress it from the anterior surface.

Schneider[4] described the typical picture of a patient with a severe hyperextension injury of the neck as that of an older person who has fallen forward on his face and head and has suffered a serious degree of tetraplegia. Facial injuries are often seen in this syndrome. Pathologic examination of tissue from the spinal cord reveals a localized hemorrhage and necrosis, most evident in the center of the spinal cord.[4] Therefore, in an injury at the C5 level there is a severer paralysis of the arms than of the legs, particularly of the small muscles of the hands, and disability often continues longer in the arms. Obviously, rehabilitation of these patients, especially the older ones, is a serious, and sometimes a discouraging, undertaking.

Berkin and Hirson[5] reported a case record pertinent to this discussion: A 64-year-old man with hypertrophic arthritis of the cervical spine received a hyperextension injury, and they had the opportunity of studying the cervical spine and spinal cord at postmortem examination. The patient had an incomplete tetraplegia, but he died of pneumonia. They were able to demonstrate the absence of bony fracture, the tear in the anterior spinal ligament, allowing hyperextension of the cervical spine to occur, the actual indentation of the spinal cord on its dorsal surface created by the bony lamina as the spinal cord was compressed against it, and the histologic sections of the recently damaged, but not transected, spinal cord. If there were doubt in the minds of some people regarding the logic of the hyperextension movement in producing cervical spinal cord trauma, this excellent presentation should adequately dispel it.

Arnold's observations[6] concerning the production of chronic spinal cord syndromes related to bony spurs of the cervical spine and the narrowed sagittal diameter of the spinal canal are also significant in acute

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injuries. Braham and Herzberger[7] more recently have surveyed this material. The studies of Wolf, Khilnani, and Malis[8] and of Boijsen[9] on the normal variation in sagittal diameter of the cervical spinal canal measured in lateral roentgenograms add further clarification. In normal cervical spines the narrowest sagittal diameter is between the lamina of C6 and the posterior-inferior edge of the body of C5. If this is further narrowed by hypertrophic spurs, the stage may be set for trauma to the spinal cord in hyperextension. The minimum measurement is commonly at C4, C5, or C6, measured between the posterior-inferior edge of the body of the vertebra, above, and the dorsal rim of the spinal canal at the base of the spinous process of the next vertebra, below. Narrowing of the sagittal diameter may be 2 mm. more in hyperextension than in full flexion. It is stated[8] that if this measured diameter is 13 mm. or less, hyperextension injuries are likely to occur; if 14 mm. or more, they are unlikely. In five patients with hyperextension injuries and with varying degrees of spinal cord damage seen recently at North Carolina Baptist Hospital, the minimum measurements were from 12 to 14 mm. The three illustrated cases are included (Fig. 3). In numerous other patients on whom measurements were made, the usual minimum measurements were 17 to 20 mm.

Occasionally with hyperextension injuries there may be gross extrusion of a cervical intervertebral disk, and manometric block of cerebrospinal fluid will be found. Surgical removal of the extruded disk is indicated in such patients. In other patients a myelographic defect from protrusion of a disk will be seen to be of such size that decompression of the spinal cord is warranted. In the experience of most surgeons[6] the cervical spinal cord can be decompressed sufficiently by doing a generous laminectomy, leaving the facets intact, opening the dura mater, and dividing the dentate ligaments, which seem to hold the spinal cord ventrally in contact with the anterior protrusion.[10,11] The majority of patients, however, do not require laminectomy, but, if performed, the rate and extent of their recovery will not be affected.

In an attempt to repeat the work of Taylor and Blackwood,[1] 3 cc. of iophendylate (Pantopaque) was introduced at the level of T2 in a cadaver, and a lateral-view, horizontal-beam roentgenogram (Fig. 1) showed this oil to be present in the dorsal portion of the canal, ordinarily considered to be a subdural or an extradural injection.

Fig. 1.—Cadaver prone—roentgenogram taken with horizontal beam. Iophendylate (Pantopaque) introduced outside arachnoid lies dorsal to spinal cord. No indentation of column in neutral position. Note degenerative arthritic spurs.

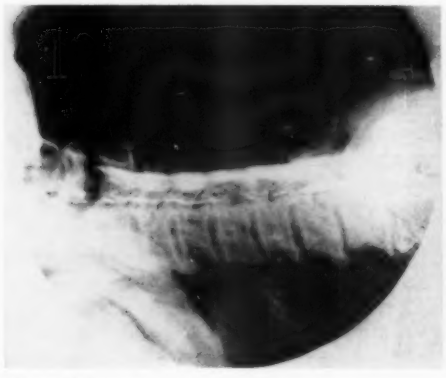

Fig. 2.—Roentgenogram taken as in Figure 1. Additional iophendylate (Pantopaque) introduced into subarachnoid space, with cadaver lying in ventral position. Neck sharply hyperextended. Note arthritic spurs protruding from ventral surface and prominent dorsal indentations of laminae and ligamentum flavum.

Subsequently, further iophendylate was introduced into the subarachnoid space through the lumbar route. The neutral-position film (Fig. 1) reveals that the column was not indented significantly; but when the neck was sharply hyperextended, there were prominent indentations, particularly from the dorsal surface. The diameter of the cervical spinal canal was reduced more than 50% (Fig. 2). When the neck was again relaxed, there was no apparent bony change, but, as Taylor has shown, in severe injuries there are often tears of the anterior spinal ligament, allowing greater hyperextension of the neck than would be possible otherwise. Occasionally ligamentous tears may be evident by the separation of a fragment from the anterior-inferior part of the vertebral body, to which the ligament is attached.

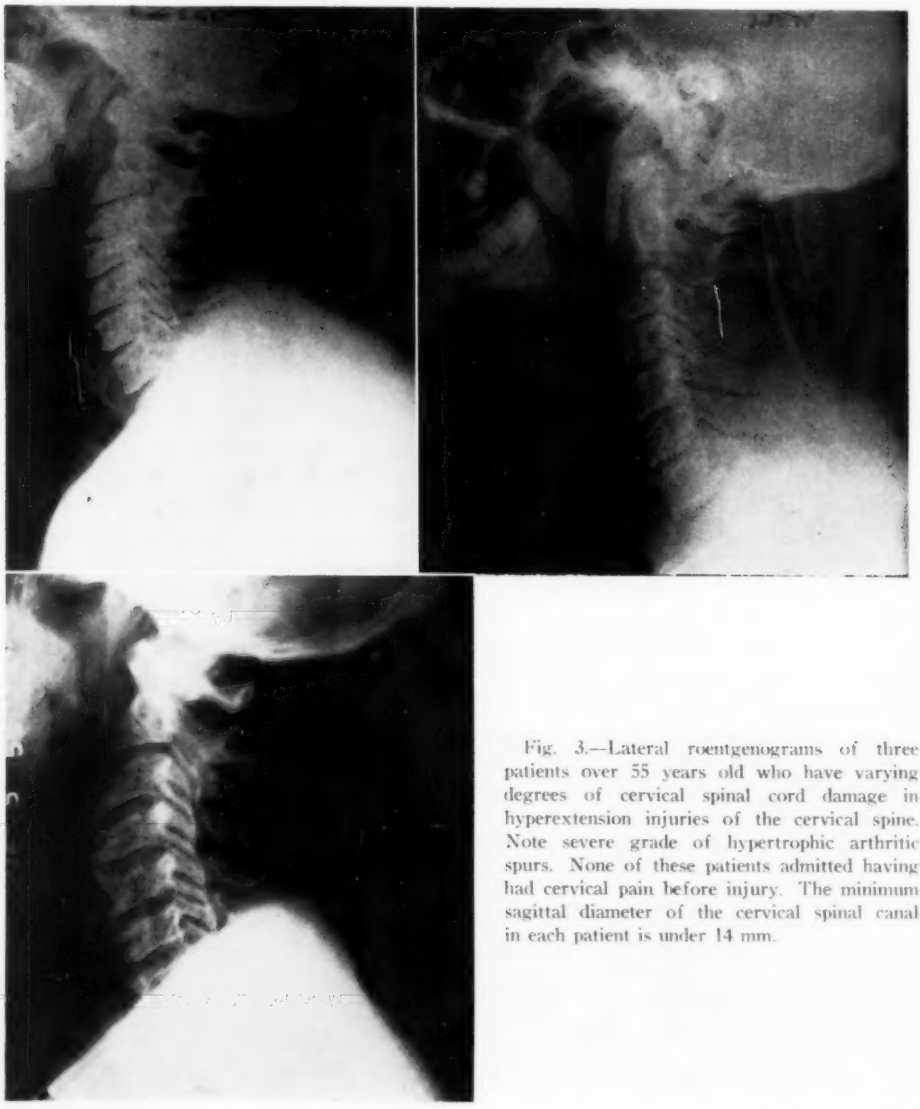

Fig. 3.—Lateral roentgenograms of three patients over 55 years old who have varying degrees of cervical spinal cord damage in hyperextension injuries of the cervical spine. Note severe grade of hypertrophic arthritic spurs. None of these patients admitted having had cervical pain before injury. The minimum sagittal diameter of the cervical spinal canal in each patient is under 14 mm.

Report of a Case

The following is the case record of a patient with a severe hyperextension injury.

A 55-year-old man fell down the cellar stairs, sustaining contusion and lacerations of his face and scalp. He was unconscious for a few minutes, and, on regaining consciousness, he was unable to move his arms. Movement of the legs was barely possible.

Physcial Examination.—He was conscious and cooperative. There was tenderness over the mid-cervical spine. Respiratory excursions were full, including both intercostal and diaphragmatic musculature. There was a vague sensory level at the C5-C6 dermatome with relative hypalgesia below that point. There was complete flaccid paralysis of both arms. He could move voluntarily all muscle groups of both legs, the left more readily than the right. There were hyperactive knee and ankle responses, positive Babinski reflexes, and sustained ankle clonus bilaterally. He was unable to void, and catheterization was necessary.

Course.—Crutchfield tongs were inserted and 10 lb. of traction was applied. Roentgenograms showed pronounced hypertrophic arthritic changes in the cervical spine but no fracture or dislocation. A lumbar puncture was done at L3 and showed a cerebrospinal fluid pressure of 160 mm. of water, a free rise to 300 mm. of water on bilateral jugular vein compression, and a rapid fall on release. The cerebrospinal fluid was grossly clear but contained 200 red blood cells on microscopic examination.

Traction was maintained for five days for comfort of the patient, after which a felt Thomas collar was applied. Ten days after injury movement began of the biceps and triceps muscles on the left side, followed five days later by a similar recovery on the right. During the next two weeks function of the bladder returned, permitting removal of an indwelling catheter. A cervical iophendylate myelogram showed no significant defect, but there were multiple small defects at the level of C4 through C7, where there were bony spurs on the plain roentgenograms.

With intensive physical therapy and training for the next month, he became able to walk alone, but disability of the arms was greater and recovery slower. There was atrophy of all the intrinsic muscles of the hands. On attempting to make a fist, he dorsiflexed the wrist because of more weakness in the flexor than in the extensor muscles of the wrist and hand.

He was able to feed himself six months after the injury, but weakness of his arms and hands was still so disabling that he could not dress himself completely or hold a pen to write.

The recovery of patients with hyperextension injuries varies with the degree of spinal cord injury; but, because of the known central location of injury to the cervical spinal cord—an area in which the the long motor tracts to the arms are more centrally located than those to the lower regions of the body—the arms, and especially the hands, suffer more than the legs. There is also local contusion to the anterior horns of the spinal cord, destroying varying numbers of the anterior horn cells. Recovery of function of the hands is likely to be slow and incomplete.

In the absence of obvious bony dislocation, manometric block of cerebrospinal fluid, or myelographic defect, there seems to be little indication for surgical intervention. Operation, if done at a later time, will reveal local scarring of the cervical spinal cord and thickening of the arachnoid membrane at the site of trauma but no other lesion favorably affected by performing surgery. A slowly progressive and continuous recovery aided by physical therapy may continue for months, or even years. These people are excellent subjects for rehabilitation.

Summary and Conclusions

The mechanism by which profound injuries to the cervical spinal cord in hyperextension may occur without fracture or dislocation is discussed.

Illustrative experiments are presented, and the roentgenograms of three patients are shown.

The importance of the sagittal diameter of the cervical spinal canal in roentgenograms in relation to cervical hyperextension injuries is emphasized.

Surgical intervention is indicated only if actual continued compression of the spinal cord is demonstrated by plain roentgenogram, myelogram, or manometric block of cerebrospinal fluid on lumbar puncture.

The long-term disability is greatest in the hands in which recovery is slowest, and rehabilitation is of paramount importance.

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The Megalencephalic Phase of Infantile Amaurotic Familial Idiocy

Cephalometric and Pneumoencephalographic Studies

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While no specific therapeutic agents have been introduced to retard the inexorable progress of amaurotic familial idiocy (Tay-Sachs' disease), adjunct measures, such as the antibiotics, have led in recent years to a protracted clinical course of this uniformly fatal infantile disorder. Thus, whereas medical texts of a few decades past mention an average life span of somewhat less than 18 months,[1-3] the 50 children in the presently reported series survived to an average age of 28 months. No deviation in the early disease phases of these cases was forthcoming to suggest any fundamental variant from the classical disease. All the children were normal at birth, displayed arrest of development before the 10th month of life, and followed a pattern of continued clinical deterioration, including macular degeneration, amaurosis, peripheral paralysis, and hyperacusis.

It was during the protracted aspect of the disease that certain features emerged which had not been associated with this illness in the past. These changes consisted, principally, of a suddenly developing and unremittent cranial enlargement, reaching extreme proportions during the extended phases of the disease.

The present paper, as a continuation of previous morphologic[4] and biochemical[5-7] investigations of amaurotic familial idiocy, is concerned with serial cephalometric and pneumoencephalographic studies of the entire scope of the disease, and a comparison of the data, whenever possible, with autopsy findings.

Source of Clinical Data

The observations presented in the accompanying Table represent the accumulated experience concerning 50 patients with infantile amaurotic familial idiocy (AFI). In 15 cases the afflicted children were permanently institutionalized shortly after the commencement of pertinent symptoms. In 11 of these cases death has supervened. An additional group, of 11 patients, who had died prior to the commencement of the present studies, were included in the statistics pertaining to the correlation of brain weight, intracranial morphology, and longevity of children with the disease. Cumulatively, therefore, 22 of the 26 children in this category have succumbed, and confirmatory autopsies have been obtained in 20 cases. In the two cases in which autopsy permission was refused, the diagnosis was based upon the classical clinical features, including the observation of retinal cherry-red spots, as well as certain serologic alterations.[6-8]

Clinical information on 24 additional cases of AFI was incorporated into the statistics, serving as comparative data for the mean figures reached for those patients characterized by unusual longevity. This last group of cases was obtained during the course of genetic studies (to be reported elsewhere) and represents corroborated, but unpublished, cases from the outpatient clinic. Of the total of 50 patients whose cases are analyzed,

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Data on Fifty Patients with Infantile Amaurotic Familial Idiocy

Case No.	Sex	Age of Onset, Mo.	Duration, Mo.	Age at Death, Mo.	Maximum Head Circumference, In.	Brain Weights, Gm.
1	M	4	13	17	Not measured	906
2	M	4	14	18	Not measured	940
3	M	6	14	20	Not measured	1300
4	M	7	23	30	Not measured	1360
5	M	6	25	31	23 1/2	1690
6	F	7	28	35	23 3/4	1520
7	F	4	33	37	23 3/4	1570
8	M	5	42	47	23 1/4	1800
9	F	5	17	22	19 1/2	970
10	F	6	30	36	19	1500
11 *	F	7	27 †		21 3/4 †	
12	F	6	24	30	19 3/4	1510
13	M	9	21	30	22	No autopsy
14 *	F	9	14 †		19 3/4 †	
15	M	8	25	33	21 3/4	1830
16	F	7	8	15	18 1/2	No autopsy
17 *	F	4	10 †		18 †	
18 *	M	8	14 †		21 3/4 †	
19	F	4	9	13	18 3/4	1070
20 *	F	7	7 †		Not measured	
21	M	4	44	48	Not measured	No autopsy
22 *	M	5	9 †		18 1/2 †	
23	M	9	9	18	Not measured	1125
24	F	8	16	24	Not measured	1070
25	F	9	9	18	Not measured	1125
26	M	6	11	17	Not measured	1230
27	M	7	16	23	Not measured	1440
28	F	9	21	30	Not measured	1160
29	M	3	11	14	19 1/4	1060
30–50 ‡	M-13 F-8	3–10	14–52	18–55	Not measured	

* Still alive.
† As of January, 1957.
‡ No cephalometric or encephalographic data on these cases.

48 were of Jewish extraction*; 22 were female and 28 were male.

In 15 cases, weekly or bimonthly occipitomental and chest circumferences were recorded for the duration of hospital stay. Pneumoencephalograms were taken at intervals of approximately six months in most cases.

Onset and Clinical Course

The age of onset in each case was often difficult to establish with precision. The appearance of an indisputable symptom was accepted as the onset, recognizing that such factors as the sensitivity of parental observation are the basis for some variation. The relative unreliability in ascribing an accurate age of onset is illustrated in Case 6. This female infant was in excellent health at the age of 7 months but underwent repeated and exhaustive physical examinations because a sibling had previously succumbed to Tay-Sachs disease. Macular degeneration was noted at this time, but no symptoms arose until the age of 9 months.

In addition, while vague prodromata, such as anorexia, were often noted in many cases and, in retrospect, probably represented the prelude of the disease, it was considered more appropriate to accept an unqualified clinical abnormality as the commencement of the illness. Inaugurating symptoms consisted of pronounced and continuing apathy, failure to recognize formerly familiar objects, limb weakness, convulsions, loss of ability to perform certain motor acts, such as holding the head up unsupported, abnormal movements, or hyperacusis.

The average age of accepted onset in the present total group of 50 cases was 5.9±0.28 months, with a range of 3 to 10 months. The relative uniformity in time of onset and symptomatic course did not carry over, however, to duration of life. Death occurred at an average age of 28.3±1.6 months, with a range of 13 to 55 months. On the basis of this spread in survival, the cases were divided, in conformity with previous studies,[4] into three groups based upon the time interval between onset and death. Group I (abortive course) consisted

* One of the two cases of amaurotic familial idiocy not of Jewish background was a Negro male infant. The diagnosis was verified at autopsy. We have found no previously published case of this disorder in a Negro.

of those 10 patients dying within 14 months of recognizable illness. Group II (average course) comprised those 14 patients surviving more than 14 months but less than 24 months, and Group III (protracted course) was composed of those 18 patients living more than 24 months after the beginning of clinical manifestations. The remaining eight children are still alive and under hospital or outpatient observation. For purposes of subsequent description, the disease has been arbitrarily separated into Phase I (first 14 months of illness), Phase II (15-24 months episode), and Phase III (period beyond 24 months of illness).

The mean age of disease onset for Group I was 6.3 months, for Group II 5.8 months, and for Group III 5.3 months. The sex ratio for the total series was approximately maintained in the individual groups. There were no initial symptoms displayed by patients of Group III which could be isolated as being a precursive indicator of a future chronic course.

Sustained clinical observations during the protracted phase of the disease (beyond 24 months of determined illness) failed to reveal any qualitative features, other than head enlargement, not repeatedly recorded in the initial years of the illness. Inanition became progressively more notable, often accentuating the head enlargement. Convulsive seizures, sometimes prominent during the early phases of amaurotic familial idiocy, tended to become subdued or undergo complete remission. A protean flaccidity and skeletal muscle atrophy evolved, and the afflicted children assumed a vegetative immobility, necessitating gastric tube feeding and periodic body rotating. Pneumonic infection and decubitus ulceration were ever-present dangers.

Cephalometric Observations

Of the 15 children with AFI serially measured and observed during the major part of their illness, 10 showed some degree of head enlargement. Of the five normocephalic children, two died within 10 months of disease commencement, and two yet alive are in an early phase of the illness. Only one infant, therefore, surviving more than 24 months of illness failed to show megalencephaly. The megalencephaly generally commenced, rather abruptly, about 18 to 21 months after the symptomatic onset. Parallel observations of chest circumference, height, and weight, on the contrary, showed no equivalent change but, rather, a retardation in accordance with the anticipated arrest of development characteristic of the disease. The discrepancy in head and chest circumference measurements, as a result, made the megalencephaly even more prominent (Fig. 1). The incremented head circumferences generally continued to increase often precipitously and progressively, until death. Normal measurements were derived from the collected statistics of Myers[9] and Watson and Lowrey[10] and corroborated in this hospital by data obtained from infants and children with non-neurologic disorders. In no instance, once megalencephaly commenced, was any prolonged cessation of enlargement or any plateau reached. At death, many of the head circumferences were about 20% above normal, indicating a cranial volumetric increase of almost twofold.

For purposes of statistical evaluation, each circumferential measurement (head or chest) was compared with the normal for

Fig. 1 (Case 15).—Clinical photograph. Male infant, aged 32 months; duration of illness, 24 months. Symmetric head enlargement; head circumference at this time, 21¾ in. (55.3 cm.)

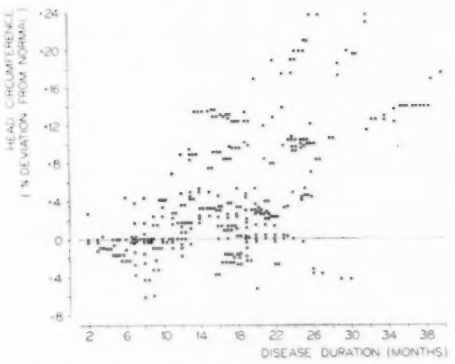

Fig. 2.—Composite graph of serial head circumference measurements in 15 cases of infantile amaurotic familial idiocy. Points expressed as percentage deviation from normal and equated to duration of disease.

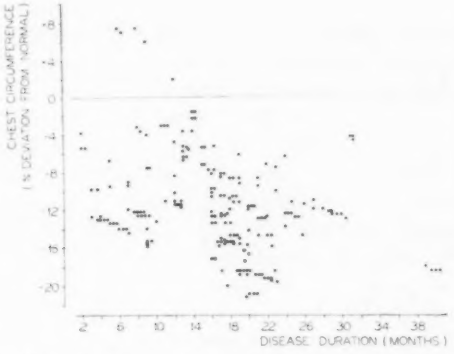

Fig. 3.—Composite graph of serial chest circumferences in 15 cases of infantile amaurotic familial idiocy. Points expressed as percentage deviation from normal and equated to duration of disease.

that age and the difference, if any, expressed as a percentage deviation from normal. Composite graphs (Figs. 2 and 3) of the 15 cases, serially followed, incorporate the individual values equated to known duration of disease. While obvious individual case variations were apparent, it is evident that normal head circumferences were characteristic of the first 14 months of the disease (Phase I). Sometime during the latter portion of Phase II, megalencephaly developed, and only one child surviving through Phase III showed normal head circumferential values. In reviewing questionnaire information derived from 15 further cases of AFI with survival of more than 24 months of illness, the parents of 10 commented upon head enlargement as a late clinical development.

Pneumoencephalographic Observations

Pneumoencephalographic studies were performed in nine patients, often serially, at different phases of the disease. In general, 45 cc. of cerebrospinal fluid was extracted from the lumbar thecal sac and 35-40 cc. of air reintroduced. The standard radiographic studies were performed after this procedure.

A uniformly abnormal pattern was noted in the pneumoencephalographic studies carried out during Phase I of the disease (Figs. 4, 5, and 6). The lateral ventricles appeared mildly dilated, occasionally one being somewhat larger than the other. The surrounding cerebral tissues appeared to be moderately atrophic, as exemplified by increased amounts of air in the supratentorial subarachnoid space. Occasionally, evidence of focal or diffuse cerebral gyral atrophy was quite prominent at this stage. Accumulations of dorsal intermeningeal air clearly outlined the retracted and shrunken gyri. The third ventricle shared in the process of dilatation. The fourth ventricle was almost invariably enlarged and clearly delineated. The basilar cisterns, particularly the cisterna magna, were unusually widened and contained a considerable amount of air. At this time there was no evidence of any increased intracranial pressure.

Studies performed during Phase II of the disease (Figs. 7, 8, and 9) generally showed a slight diminution of the formerly existent lateral ventricular dilatation. The cerebral cortical atrophy, so often observed in the initial aspects of the disease, now also tended to regress. Where diffuse pockets of intergyral subarachnoid air had previously been noted, no such radiographic findings were now visualized. The marked degree of dilatation of the fourth ventricle observed during Phase I was again recorded,

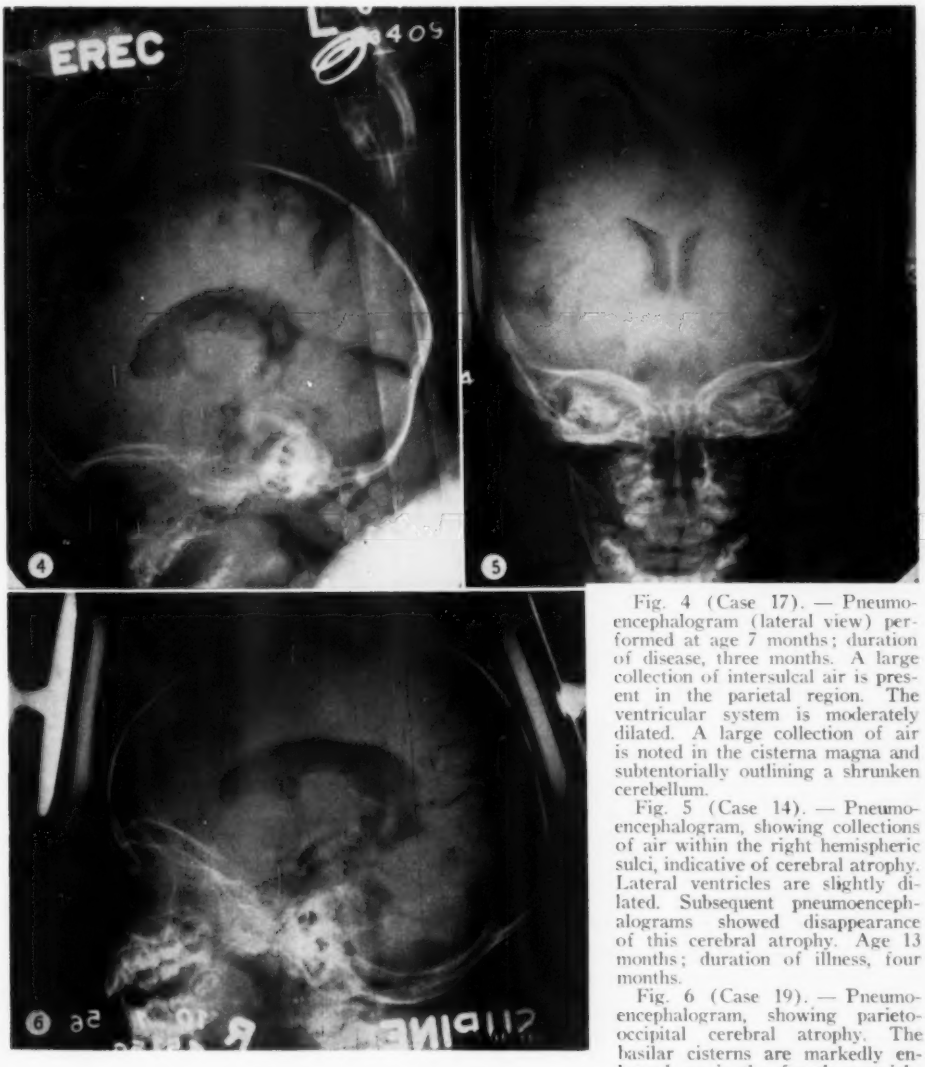

Fig. 4 (Case 17). — Pneumoencephalogram (lateral view) performed at age 7 months; duration of disease, three months. A large collection of intersulcal air is present in the parietal region. The ventricular system is moderately dilated. A large collection of air is noted in the cisterna magna and subtentorially outlining a shrunken cerebellum.

Fig. 5 (Case 14). — Pneumoencephalogram, showing collections of air within the right hemispheric sulci, indicative of cerebral atrophy. Lateral ventricles are slightly dilated. Subsequent pneumoencephalograms showed disappearance of this cerebral atrophy. Age 13 months; duration of illness, four months.

Fig. 6 (Case 19). — Pneumoencephalogram, showing parieto-occipital cerebral atrophy. The basilar cisterns are markedly enlarged, as is the fourth ventricle. Age 10 months; duration of illness, six months.

sometimes to an even greater extent. The atrophy of the infratentorial structures apparently became more pronounced during this phase, and surrounding subarachnoid air clearly demarcated the cerebellum.

Pneumoencephalograms performed during the protracted stage of illness (Phase III) showed a number of changes distinguishing it from the antecedent phases (Fig. 10*A*, *B*). The bulk of supratentorial tissues was significantly increased, as determined by the extent of radiopacity between the lateral ventricular borders and the calvarial demarcation. The degree of dilatation of the lateral ventricles usually diminished, although in two cases the enlargement continued. The amount of air in the basilar cisterns remained approximately the same,

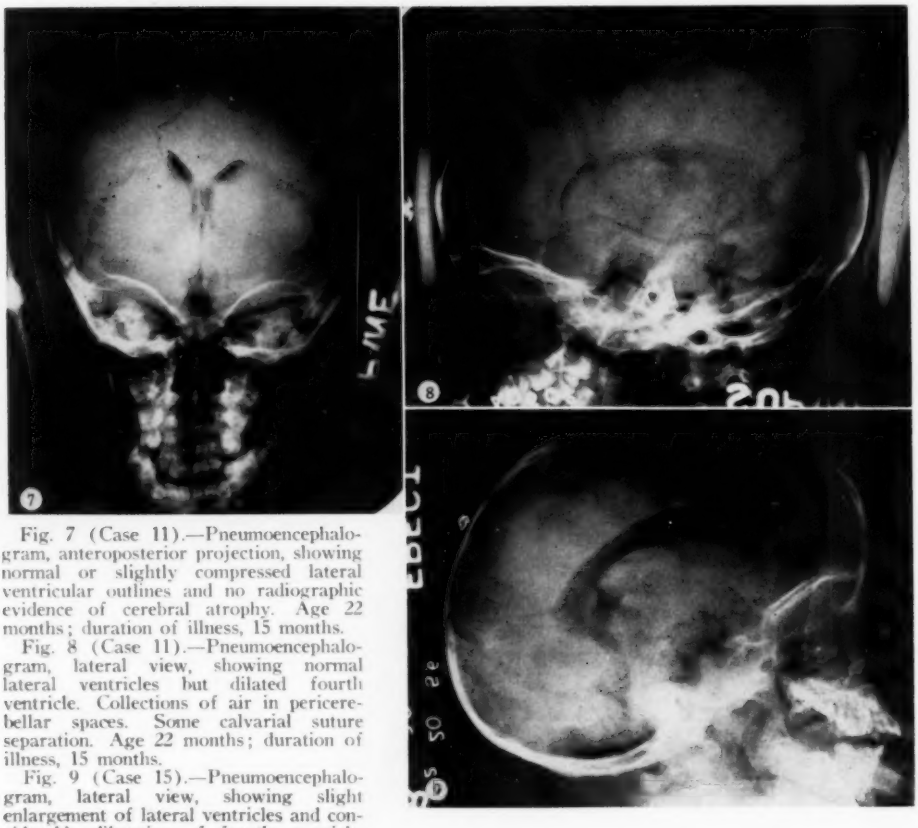

Fig. 7 (Case 11).—Pneumoencephalogram, anteroposterior projection, showing normal or slightly compressed lateral ventricular outlines and no radiographic evidence of cerebral atrophy. Age 22 months; duration of illness, 15 months.

Fig. 8 (Case 11).—Pneumoencephalogram, lateral view, showing normal lateral ventricles but dilated fourth ventricle. Collections of air in pericerebellar spaces. Some calvarial suture separation. Age 22 months; duration of illness, 15 months.

Fig. 9 (Case 15).—Pneumoencephalogram, lateral view, showing slight enlargement of lateral ventricles and considerable dilatation of fourth ventricle. No cortical subarachnoid air noted. Age 23 months; duration of illness, 15 months.

and the radiographically determined infratentorial atrophy persisted through Phase III. Invariably, however, the amount of cerebral substance was markedly augmented during this phase, and a very obvious cranial expansion was verified roentgenologically. Fontanelles were occasionally still open, often displaying a wide degree of separation.

Pathologic Findings

Complete pathologic data were available in 20 cases. The brain weights of all autopsied patients were individually compared with the anticipated normal measurements for the pertinent age and sex as established by the accumulated organ weight statistics of Coppoletta and Wolbach [11] and others.[12] Alterations from normal were expressed as a percentage deviation and graphically equated with the duration of illness (Fig. 11). During the initial phase of the disease, eight deaths occurred. Brain weights in this category were generally normal, or in some instances slightly below normal. Derived specimens during this phase at times showed a moderate but visible gyral atrophy. The gyri were abnormally contracted, often exposing the sulcal depths. Dissection of such specimens frequently disclosed a moderate, and usually symmetrical, ventricular dilatation. The leptomeninges were visibly opaque, but no exudate was seen. The underlying cerebral substance was frequently

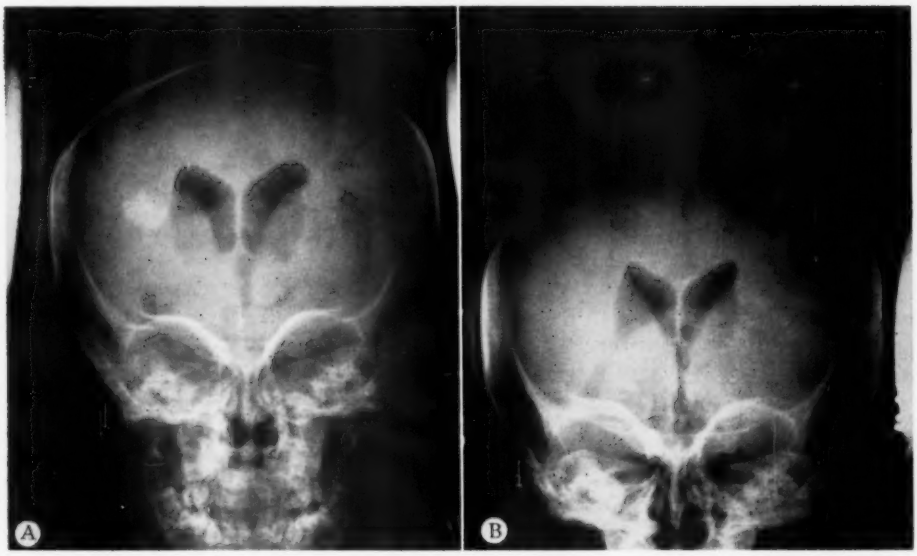

Fig. 10 (Case 10).—*A*, pneumoencephalogram, disclosing zones of cerebral cortical atrophy and moderate enlargement of the lateral ventricles. Age 19 months; duration of illness, 13 months.

B, pneumoencephalogram, showing an increase of supratentorial brain tissue, reduction in ventricular size, and absence of radiographic evidence of cerebral cortical atrophy, as contrasted with *A*. Age 35 months; duration of illness, 29 months.

denser than normal, reflecting the moderate degree of secondary gliosis usually observed in this phase of the disease. The infratentorial tissues (brain stem and cerebellum) shared the process of atrophy characteristic of the cerebral hemispheres. The fourth ventricle was usually enlarged, as was the aqueduct of Sylvius. However, there was no evidence of any obstructive lesion to which the ventricular enlargement could be attributed.

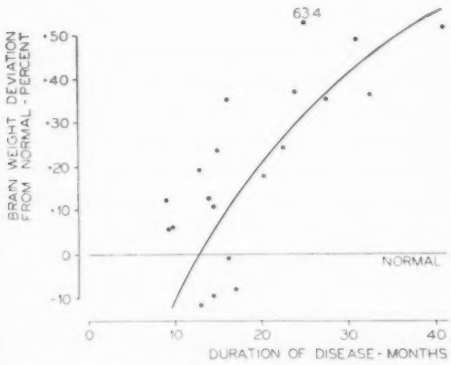

Fig. 11.—Brain weights in 20 autopsied cases of infantile amaurotic familial idiocy. Weights expressed as percentage deviation from normal and plotted against duration of disease.

Histologically, during this phase, there was ubiquitous involvement of the ganglion cells at all levels of the neuraxis, although some segmental variations were apparent.[4] The hemispheric white matter was generally intact, although some zones of frontal-lobe pallor were revealed by myelin-stain preparations.

In the six children who died during Phase II of the disease brain weights were either normal or slightly above anticipated normal. The characteristic supratentorial gyral atrophy noted previously was no longer evident. Brain specimens were of approximately normal proportions, and operculization was no longer a prominent external feature. The leptomeningeal fibrosis was again observed to a moderate but irregular degree. The infratentorial tissues, in contrast, persisted in showing atrophic contraction.

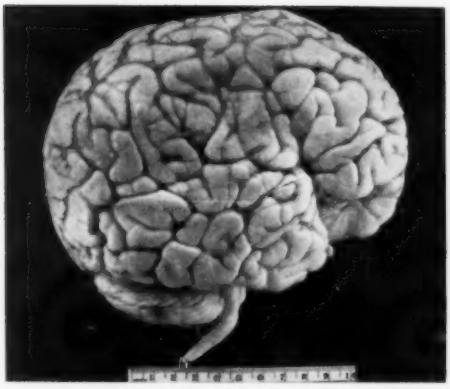

Fig. 12 (Case 15).—Lateral view of undissected brain. Note considerable expansion of cerebral hemispheres and the deceptive gyral voluminousness. In contrast, the cerebellum and brain stem are visibly atrophic. Age 33 months; duration of illness, 25 months. Compare with Figure 1.

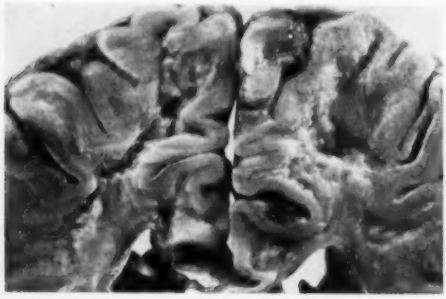

Fig. 13 (Case 8).—Coronal section of brain, showing bilateral foci of extensive demyelination and cystic degeneration.

In the six children who died during the protracted phase of amaurotic familial idiocy, brain weights were uniformly above normal. In general terms, the more prolonged the clinical course the greater the degree of abnormal weight expansion. Brain weights up to 1830 gm. were recorded in children surviving as much as three years after the onset of the disease. Both cerebral hemispheres were unusually and uniformly voluminous and the component gyri full and tense (Fig. 12). There was no evidence of any focal atrophy or abnormal widening of the sulci. On the contrary, the sulcal crevices were unduly compressed. The leptomeningeal thickening was still in evidence but did not show any significant increase beyond that observed in the previous phases. In distinct contrast, the cerebellum and brain stem exhibited a marked atrophy, such that the disparity between supratentorial and infratentorial structures was further exaggerated. The cerebellum and brain stem gave the appearance of vestigial appendices to the hugely enlarged cerebral hemispheres.

Serial cross sections through the affected cerebral hemispheres showed a repetitive pattern in all the specimens derived from children succumbing during Phase III of the disease. The ventricular cavities were of normal dimensions, or occasionally compressed, and in one case slightly enlarged. The bulk of cerebral tissue, however, was inordinately increased. This increment was exclusively within the white matter. The frontal and posterior parietal white matter was considerably expanded and showed a peculiar form of coalescent cystic necrosis, characterized by ragged, irregular zones of encephalomalacia and surrounded by marked demyelinated and edematous tissues (Fig. 13). The demonstrable demyelination extended far beyond the central zones of cavitary necrosis, encroaching upon the cortical mantle. The normally visible line of distinction between cortical gray matter and subjacent white matter was totally obscured at this stage of the disease. In addition, focal zones of linear encephalomalacia were observed within the presumed area of gray matter.

Histologically, the cortical mantle of the cerebral hemispheres displayed a diffuse and marked ganglionic involvement inherent in the disease. However, in contrast to previous stages of the illness, most neurons had now degenerated completely, leaving whole fields of cortex with no residual neurons, but solely a secondary and extensive glial responsiveness. The axonal prolongations of the lysed neurons showed a secondary degeneration, with degradation of the encompassing myelin sheaths within the deeper white matter, eventuating in a diffuse tissue breakdown throughout the subcortical tis-

sues. In response to this generalized degeneration, there was noted an overwhelming glial reaction within the white matter. This hyperplasia of glial cells occasionally appeared to be out of proportion to the anticipated response to axonal degeneration. Many of the secondary, proliferating astrocytes revealed multinucleation and visible cytoplasm. In contrast, the tissues comprising the cerebellum merely showed an extended pattern of neuronal ballooning, but no devastating degree of cell necrosis or superimposed glial responsiveness typifying the cerebral changes.

Comment

In the first comprehensive publication concerning amaurotic familial idiocy, Sachs designated the disease as one of "arrested development." [13] His description was based upon the clinically observed cessation of somatic growth, the associated loss of functional activity, and the finding of an atrophic brain at autopsy. Subsequent studies by other investigators of the disease have reaffirmed the primacy of central nervous system degeneration.[14-16] Numerous authors have repeatedly described the typically shrunken, diffusely gliotic brain specimens presumably specific for this disease. The majority of such patients, however, died well within two years of the first clinical sign of amaurotic familial idiocy.

A fundamental question arises as to whether the clinically prolonged cases comprising the presently reported series represent valid instances of infantile amaurotic familial idiocy. In the light of this, a comprehensive comparison of the classically described disease and the current group would be warranted. In 1933 Slome reviewed 127 confirmed cases of amaurotic familial idiocy gathered from published data.[17] His statistics indicate that the average age of clinical onset to be 5.8 ± 0.3 months, a figure in close accord with the total average of 5.9 ± 0.28 months noted in the presently reported series.

All the afflicted children displaying the undue longevity in the present series were Jewish, in conformity with the acknowledged genetic substrate of the disease. The familial nature of the illness, as portrayed by sibling penetrance,[1,17,18] was recorded in the prolonged cases, as well as in our cases in which the child survived only the anticipated period of time.

Other authors have designated three to eight months as the average time of disease inception. The relatively trivial variations among the various reported series may only reflect the astuteness and sensitivity of parents to neurologic abnormalities in their children. Some authors may consider onset as the time when the disease was firmly diagnosed (e. g., macular degeneration). Others may diligently search for precedent symptoms, which assume importance only in the light of subsequent developments. The point may be academic, since some observers feel that the disease is present at birth, and that its detection often rests upon the fortuitous presentation of a dramatic symptom, such as convulsions.

In the present series, the time and mode of onset does not differ materially between the 18 patients of Group III and the remaining patients with more abbreviated duration, or the cumulative descriptions of the disease in the medical literature. Predominant symptoms and signs in the presently considered protracted group included progressive amaurosis, macular degeneration, diminished motor capacity, tetraplegia, arrested development, hyperacusis, idiocy, convulsions, and marasmic inanition. This symptom complex constitutes an almost precise reproduction of Sachs' clinical criteria of the disease bearing his name. No additive symptoms emerged in our patients of Group III, other than late megalencephaly. In Slome's series [17] the survival age averaged 18.6 ± 0.9 months (i. e., average duration of recognized illness, 12.8 months). Globus [16] considered 21 months as the average age of death, and others have mentioned

16 to 22 months as representative of their experience.

A later review of the disease by Rothstein and Welt [19] again concludes that the duration is about 18 months, but these authors allude to four previous reports of cases with a more protracted course. They specified, however, that in each of these prolonged cases the disease was atypical. No cherry-red spot was found, but other macular changes were present (e. g., retinitis pigmentosa), possibly representing "equivalents." The cases of prolonged duration in the present series, however, all displayed the classical retinal cherry-red spots.

Age at death in our series was 28.3 ± 1.6, with 18 patients living beyond 24 months. The longest duration of life (55 months) was observed in Case 41. Of the eight living children presently under clinical observation, four have survived more than 21 months beyond the first symptom and two 36 months beyond.

There can be no confusion between the protracted cases of infantile amaurotic familial idiocy and the late infantile (Jansky-Bielschowsky) form of AFI. The latter cases, while generically associated with the infantile form generally, do not commence before the third year of life, rarely show macular degeneration but, rather, exhibit primary optic atrophy or retinitis pigmentosa, and do not display the selective racial predilection characteristic of infantile amaurotic familial idiocy.[2,20,21] In addition, pathologically, the characteristic changes of the protracted phase described above have never been noted in the late infantile form of the disease.[22,23]

The collective observations recorded in this paper appear to be initially contradictory. In a progressive disease eminently degenerative in nature, the sudden, but tardy, emergence of cranial enlargement would seem to indicate the introduction of an independent disease or a variant of sufficient import to remove such cases from the general category of amaurotic familial idiocy. A further careful examination of the medical literature dealing with this illness, however, discloses isolated instances of identical or similar nature (i. e., prolonged course and late megalencephaly). Schaffer mentions a typical case in a Jewish female infant succumbing at the age of 26 months and terminally showing both cranial enlargement and, at necropsy, a voluminous cerebrum associated with secondary white matter degeneration, almost identical with that described above.[24] Gourley and Wigglesworth describe a male infant who had beginning symptoms at 7 months and survived until 33 months of age.[25] The head circumference in this child at death was 20 in. (normal, 18.8 in.). Cranial suture separation and calvarial thinning were also noted in this case. These authors briefly alluded to another case, persisting until 30 months of age. Ostertag also published a case with an unusual prolongation of the clinical symptoms and with cranial enlargement, as well as megalencephaly.[26] De Silva and Tennekoon [27] reported two cases surviving 34 and 26 months, respectively. Bird describes a case with increased head circumference and demonstrable megalencephaly (1250 gm.) at autopsy.[21] Einarson reported a typical instance of amaurotic familial idiocy with diffuse hemispheric demyelination, including the arcuate fibers, and intense gliosis.[28] He interpreted his case as a transitional form between amaurotic familial idiocy and diffuse sclerosis. A further case report concerned with the endocrinologic aspects of amaurotic familial idiocy mentions "hydrocephalus" in a 22-month-old infant.[29] It is thus evident that, while cases surviving beyond 18 months of illness are unusual, the occurrence is by no means rare and does not justify a separation on the basis of unusual prolongation of life.

Prior to autopsy evaluation, it was felt that the critical head enlargement may be attributable to an obstructive hydrocephalus. This notion was strengthened by the preliminary findings of slight or moderate ventricular dilatation demonstrated in the

early aspects of the disease by pneumoencephalography. Such a finding of ventricular dilatation in this disease has also been noted by others.[16] Some published autopsy reports of patients succumbing within 2 years of age have described an incipient internal hydrocephalus.[30] Russell has noted an extensive obstructive hydrocephalus in an autopsied case of gargoylism,[31] a remotely related dystrophic storage disorder involving also the central nervous system. In her reported case, the leptomeninges were diffusely fibrosed, thus impeding the flow of cerebrospinal fluid and resulting in ventricular dilatation. The subarachnoid fibrosis was caused by the continuing transportation of lipid detritus through the perivascular spaces of Virchow-Robin into the leptomeninges, provoking a progressive mesodermal reaction. Other descriptions concerning the pathology of gargoylism confirm this observation.[32]

In most of the presently reported autopsied cases of amaurotic familial idiocy a qualitatively comparable subarachnoid alteration was seen, grossly represented by a diffuse surface opacity.[33] Histologically, the mobile phagocytes were noted in large numbers throughout the perivascular system and could be traced with ease through the subarachnoid cavity. The arachnoid trabecular cells appeared to inaugurate the action, becoming hypertrophied and assuming a phagocytic role. Some fibroblastic and capillary proliferation followed. In none of the present cases studied, however, was this leptomeningeal fibrosis as striking or paramount as in Russell's case of gargoylism.[31] The mild ventricular dilatation indicated by pneumoencephalographic studies and confirmed in some of the autopsies in cases of AFI may be caused in slight measure by this pericerebral fibrosis.

As survival was prolonged and head enlargement proceeded in unabated fashion, the concept of internal hydrocephalus due to meningeal obstruction became untenable. This was particularly true when subsequent serial pneumoencephalograms failed to show a degree of ventricular volume increase comparable to the magnitude of cranial enlargement. In many instances, the ventricles actually diminished in size as the external cranial dimensions expanded. Occasionally, striking cerebral cortical atrophy was demonstrable by pneumoencephalography early in the course of the illness, followed by a regression of this cortical atrophy and secondary expansion of the intracranial tissue volume.

Autopsy of brains derived from the present series of patients with amaurotic familial idiocy corroborated the impression that the indisputable head enlargement characteristic of the protracted phase was not a reflection of internal hydrocephalus but, rather, an actual increase in brain tissue substance. The 20 autopsied cases of this series were evaluated on the basis of brain weight. In afflicted children succumbing early in the course of the disease (i. e., less than 14 months of clinical illness) the brain weights were normal or less than normal. Children succumbing at a later date showed a significant and continuing deviation from normal, the brains becoming more and more voluminous as the duration lengthened.

It became apparent that an ostensibly paradoxic reversal in disease evolution ensued. An unremitting cerebral atrophy proceeded conjointly with, and was attributable to, a continuing dystrophic storage disorder implicating the central nervous system ganglion cells. The cerebral atrophy exhibited in the early phases of the disease, and commented upon repeatedly in appropriate medical descriptions, probably antecedes the retardation of growth prompted by the reduced functional capacity of the central nervous system ganglion cells. It is clinically ascertained that function of the implicated nerve cell is not totally abolished, since the vulnerable intracytoplasmic neurofibrillary network is not destroyed until very late in the course of the cell ballooning. Thus, Sachs' term "arrested development" may be more accurately termed "suppressed devel-

opment," in keeping with the above observations.

Some have contended that the disturbance of lipid metabolism is already present in limited fashion at birth and produces symptoms only after months of continuing intracellular ganglioside accumulation. The first phase of the disease may then be considered as a stage of progressive intraneuronal infiltration, partial malfunction of involved ganglion cells, retardation of the capacity for further development with mild or moderate attendant cerebral atrophy, but no significant breakdown of the altered and diseased nerve calls. When the critical point in the relentless storage process is reached, a diffuse and approximately simultaneous neurocytolysis is precipitated, resulting in a structural loss of large numbers of ganglion cells. This undoubtedly causes a secondary breakdown of the axonal appendices with their protective myelin sheaths. A devastating cerebral white matter demyelination ensues, often simulating the gross morphology of Schilder's disease and accompanied by an overwhelming edema and reactive gliosis. The liberated, abnormal lipids may contribute to the disparate dimensions of the glial response. As a consequence, the cerebral hemispheres reexpand, achieving m e g a l e n cephalic proportions, which in reality only represent an overwhelming and protean gliogenous hyperplasia.

Curiously, the cerebellum and brain stem continue to atrophy even in the protracted aspect of the disease. This is preeminently demonstrable in both air-contrast x-ray and autopsy studies. At no time, however, does the degree of actual cell breakdown in the infratentorial tissues ever approximate that exhibited in the cerebral hemispheres. The Purkinje cells of the cerebellum are markedly involved, but the quantitatively more numerous granular-layer cells never exhibit the distended configurations or cell destructions characteristic of the cerebral ganglion cell gray matter mantle. Similarly, there are many brain stem nuclei (e. g., inferior olivary nuclei) which show only a modicum of dystrophic involvement, even after years of clinically evident disease. These observations seem to support the previously advanced hypothesis that an approximate parallelism exists between ontogenetic development and degree and extent of neuronal involvement. Consequently, the most recently developed cerebral areas are the most vulnerable to the disease process.[4]

Summary

The present report represents a segment of a comprehensive study of 50 patients with infantile amaurotic familial idiocy and is specifically concerned with serial cephalometric and pneumoencephalographic observations on 15 of these cases. The findings were projected against the necropsy data of 20 cases of this series. In many of the children, the duration of life was significantly prolonged, culminating in massive megalencephaly, a feature not sufficiently acknowledged in the past. This was evident in a markedly increased head circumference, as well as increase of brain mass, visualized radiographically and at autopsy.

Morphologic studies helped to clarify the paradox of an enormous increase in brain weights in the presence of progressive neuronal degeneration. It was observed that the late megalencephaly was the result of a reactive glial overcompensation and hyperplasia.

Dr. Abram Kanof aided in diagnosis and selection of patients for this study.

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Effect of Midbrain Lesion on Experimental Allergy

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The role of the central nervous system in the development and course of anaphylaxis has received relatively little recent experimental attention.[9,13] At the turn of the century, pioneer investigators considered the brain to be the target organ initiating the reaction, until experiments demonstrated components of the syndrome in the presence of decerebration and decapitation.[1,20,21] Knowledge of the immunologic and biochemical aspects of anaphylaxis has since been extensively advanced, but neural factors in the syndrome remain to be delineated.

Closely resembling human asthma, anaphylactic shock in the guinea pig terminates in a relatively sudden respiratory death. The release of H substances (histamine, acetylcholine, or anaphylatoxin) in the antigen-antibody reaction results in bronchospasm. Autopsy reveals emphysematous lungs fixed in deep inspiration as a consequence of spasm, edema, and mucous exudate. Bronchospasm occurs in vitro in the presence of histamine. In the intact animal this reaction may be modified because the release of H substances presents a physiologic crisis calling for a variety of adaptive responses. For the integrated performance of physiologic and behavioral adaptation the participation of the central nervous system would be required.

The hypotension and bronchospasm of anaphylaxis should be and are compensated by increased sympathetic activity. The developing oxygen deprivation appears to be linked to active and excited air-searching behavior. The animal may die because these adaptive efforts are not specific and are predominantly directed toward relieving air deprivation rather than bronchospasm. To an internal crisis, the animal responds as though the danger were externally located. This projection represents a primitive "error" in adaptation; in consequence, the alerted animal employs a predominantly somatic mechanism to relieve a visceral disorder. We thought, therefore, that alteration in central systems integrating somatic and visceral functions would permit the adaptation to be directed more effectively toward the vital source of difficulty.

While the bronchorelaxant effect of epinephrine and atropine are well known, knowledge of peripheral autonomic status does not elucidate the central mechanisms involved. The reticulum of the brain stem does not represent a central autonomic center but, rather, is a substrate mediating a complex of somatic and visceral sensorimotor adjustments. Further, the activity of the reticulum is related to alertness, or the readiness of motor, autonomic, and higher neural systems to respond.[6] If one assumes that this internuncial system of the brain stem participates in the regulation of activities of adjacent and distant nuclei, its disruption might alter the pattern and course of anaphylactic behavior by inhibiting the readiness to respond to bronchospasm with air-searching behavior. A variety of anesthetic agents may protect the guinea pig from anaphylactic death.[2,10,19] Since the action of anesthetic agents has been linked to the function of the midbrain reticulum,[12] we thought that lesions in a selected part of this area in particular might alter the manifold of regulatory mechanisms so as to protect the animals from death.

Methods and Materials

A group of 22 guinea pigs were sensitized by an intraperitoneal injection of egg albumen; 2 mg.

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of the protein in 2 cc. of water was administered daily for two successive days. After allowing two weeks for the formation of antibodies, 16 of the animals were operated on under light ether or pentobarbital (Nembutal) anesthesia. Bilateral brain stem lesions were produced by electrocoagulation. A stereotaxic instrument designed for the cat was with some difficulty adapted for the guinea pig, while coordinates were interpolated from Krieg's atlas of the rat brain.[14] A needle electrode was placed successively on each side of the brain for 20 seconds while a current of 2 amp. was passed from its exposed tip. The second pole was attached to the shaved abdomen. Twenty-four hours postoperatively a challenging dose of 2 mg. of albumen in 0.5 cc. of sterile water was administered to all animals by intracardiac injection. The guinea pigs were not under any anesthetic restraint at the time of the cardiac puncture. An intraperitoneal challenge may also be used to initiate anaphylaxis, but the slow absorption of the large protein molecule may delay the commencement of the syndrome for many minutes. Postmortem perfusion was accomplished with a 10% solution of formaldehyde, and serial sections of the brain were prepared with thionine, iron, and Giemsa stains.

Results

A characteristic succession of symptoms occurs in the sensitized control animals. Twenty seconds following intracardiac challenge the animal may appear unaffected. Then he vigorously scratches his nose, sneezes, chomps, and shows ruffling of hair and rapid eye blinking, behaving as though the nasopharyngeal tract is irritated. These symptoms increase and tachypnea is observed. Within two minutes, signs of air hunger are prominent and one sees searching movements, the animal appearing to sniff or "taste" air, or to explore with more or less excitement the corners of the enclosure. The expiratory movements become forced and labored; rales increase in audibility, and the nares may show mucous or frothy exudate, the eyes watering. Excessive motor activity ensues, the animal running and jumping, while cyanosis is clinically evident. Now, in acute respiratory embarrassment, he halts and makes desperate gasping attempts until he buckles, falling supine. Clonic convulsive movements may sometimes be observed. The gasping animal becomes apneic; all respiration finally ceases, and cardiac failure follows in a matter of minutes. Two to six minutes following the challenge the animal is dead.

In 7 of 16 animals operated on stereotaxically we succeeded in placing bilateral lesions in the reticulum. Six of these animals showing similar lesions survived, while the lesion in the seventh animal (No. 10) was at a more caudal level. In the surviving animals, the onset of symptoms was reminiscent of the typical shock reaction. However, the syndrome never did progress beyond the stage of nasopharyngeal irritation. The animals might chomp, blink, and ruffle; but the scratch component was infrequently observed. No signs of motivated air hunger were observed. Two animals appeared slightly cyanotic but did not act as though they were uncomfortable. Most showed moderate tachypnea with occasional rales for a period of three to six minutes. No running movements and no indications of respiratory embarrassment were observed. Animals were killed one hour or more after the challenge. During the period of observation, remission of symptoms occurred, and there was no further clinical evidence of the effect of anaphylaxis. While we anticipated sleep, none of the animals were drowsy; indeed, they appeared as alert and reactive as the controls. Results are summarized in the accompanying Table.

These animals had a common lesion, as depicted in the Figure. This lesion appears to interrupt portions of the midbrain reticulum involving the reticulothalamic tracts and deep tegmental nucleus. The rostral-caudal extent of the lesion (in a plane parallel to Krieg's stereotaxic coordinates) is limited to the caudal border of the superior colliculus and extends rostrally to the mid level of the superior colliculus.

Ten animals operated on exhibited typical anaphylactic shock and died within two to six minutes after the challenge. In no instance were the lesions identical with the preceding group, although one animal (No. 10)

Comparison of Survival Time and Site of Lesion

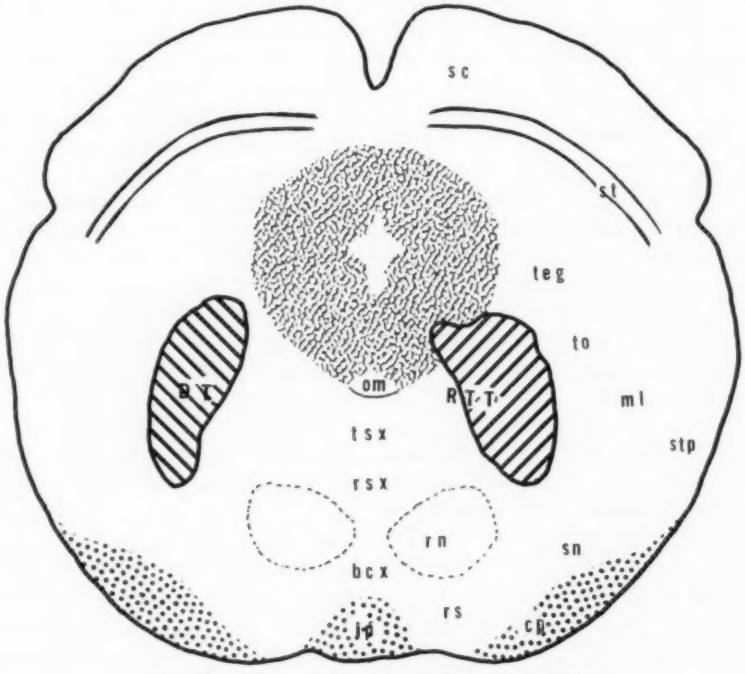
No. of Animals	Site of Lesion	Survival Time, Min.
6	Midbrain reticulum at midlevel of superior colliculus (Figure 1)	60*
6	Nonoperative controls	2-6
1	Reticulum at level of inferior colliculus (No. 10)	4
2	Cerebral peduncles	5
1	Substantia nigra on right, tectum on left	3
1	Midbrain reticulum on right, peduncle on left	4
2	Central gray matter at level of brachium pontis	3
1	Trapezoid body	6
1	Tectum at level of superior colliculus	5
1	Unilateral in posterior hypothalamus	4
1	Bulbar reticulum	60*

* These animals, in good condition, were killed after one hour.

had bilateral reticular lesions at a more caudal level. Lesions in 4 of the 10 animals were at the same rostral-caudal level as that of the surviving group. Of these four, two animals showed bilateral destruction of the cerebral peduncle and no impingement on midbrain reticulum. One animal had a unilateral lesion in the substania nigra and, contralaterally, partial destruction of the tectum. The fourth animal showed a lesion in the reticulum unilaterally, while the contralateral lesion involved only the peduncle.

Three animals showed destruction at various levels of the inferior colliculus, in two of these involving midline lesions in the central gray matter at the level of the brachium pontis. The third animal (No. 10) showed destruction of reticulum bilaterally at the rostral level of the inferior colliculus. The rostral-caudal extent of the lesion is limited to this level, which is caudal to the nucleus of the fourth cranial nerve.

The eighth animal had bilateral lesions in the trapezoid body, and the ninth, a bilateral lesion in the tectum at the caudal



Composite cross section of survival group lesion.

Diagonal lines indicate lesion. *bcx*, decussation of brachium conjunctivum; *cp*, cerebral peduncle; *DT*, deep tegmental nucleus; *ip*, interpeduncular nucleus; *ml*, medial lemniscus; *om*, nucleus of third nerve; *rn*, red nucleus; *rsx*, decussation of rubrospinal tract; *RTT*, reticulothalamic tract; *sc*, superior colliculus; *sn*, substantia nigra; *st*, spinotectal tract; *stp*, lateral forebrain bundle; *teg*, lateral tegmental nucleus of midbrain; *to*, tecto-olivary tract; *tsx*, tectospinal decussation.

Modified after diagram in "Comparative Neurology," by J. W. Papez,[16] published by Thomas Y. Crowell Company, New York, 1929.

level of the third ventricle. The 10th animal showed a unilateral lesion in the posterior hypothalamus, dorsal to the mammillary body at the level of the geniculate bodies.

In one additional animal, a bent hypodermic needle was manually inserted and moved across the brain stem. The animal exhibited hyporeactivity, hyporeflexia, and a rigidity in all extremities, with fine tremor. Generally unaware, the animal would show spurts of activity on arousal (running movements while lying on his side). After challenge, he lay quietly on his side, and, though showing none of the preliminary anaphylactic symptoms, he did exhibit a mild cyanosis with wet, slow, regular breathing. These symptoms persisted without change for two hours, at which time he was killed. Histologic study revealed bilateral destruction of the bulbar reticular nucleus and the rostral portion of the respiratory nucleus. Lesions were lateral to the medial lemniscus at the level of the nuclei of the sixth nerve and the acoustic tubercle.

Comment

These results indicate that critically placed, bilaterally symmetrical lesions in the midbrain reticulum can inhibit the full-blown syndrome of anaphylaxis and ensuing death. Two descriptive phases of the syndrome emerge from these procedures: an initial phase, of nasopharyngeal and tracheobronchial irritation with tachypnea, and a second, lethal phase, of hyperpnea, excitement, and expiratory pumping. While the lesion may have modified the severity of components of the first phase, it clearly inhibited the development of the second phase. The status of central neural systems can be experimentally linked to the development and course of an allergic syndrome, but neither the specific pathophysiologic components affected by the midbrain lesion nor the possible range of consequent behavioral alterations is revealed by our methods.

Possible component mechanisms by which the syndrome could have been altered bear consideration. The lesion, through autonomic connections, may have produced a tonic background in smooth muscle, against which H substances would be less effective in inducing spasm. A parallel possibility lies in an effect of the lesion upon the development of wheals. Wheal formation depends on the arteriolar dilating effect of an axone reflex fired antidromically by H substances. Selective stimulation of the reticulum has been shown to influence antidromic firing and potentials,[4] and diencephalic and central lesions have been reported to affect the degree of wheal formation,[5,10] so that it is possible that the lesion diminished the amount of transudation and local obstruction. Two different mechanisms related to the reticulum may, therefore, have dampened the effect of H substance on smooth muscle and inhibited the full development of the syndrome. These possibilities refer mainly to the first phase and diminished capacity for peripheral response as an effect of the lesion.

Events of the second phase—sudden hyperpnea, forced expiration, excitement, and air searching—appear to increase the mucous exudate, obstructive emphysema, and anoxia, which lead to death. In terms of central events, we do not know how these mutually exacerbating processes are related, but such overactivity appears to diminish the effectiveness of regulatory mechanisms. Essentially, a facilitation of expiratory secretory and motor mechanisms is involved in the second phase; the medullary lesion may have blocked such facilitation at one of a series of crucial levels. This facilitation and the search for air cannot be triggered by anoxia per se,[8] although carbon dioxide excess could contribute to sustaining the excitement. Epinephrine, acting on reticular substrate, can activate these neurones, and this may have bearing on the lack of excited behavior with the lesion.[3,7]

The chief peripheral event in anaphylaxis is, however, bronchospasm, and it is known that sudden hyperpnea and forced expiration can be elicited when there is an increase in bronchial stimulation, which would be transmitted to the medulla.[8] Papez [17] has sug-

gested that from the medulla the relay of afferent vagal impulses courses through the destroyed area. This area may be diffusely stimulated by afferent relays, may augment the afferent input, and may be linked with a variety of adaptive mechanisms directed toward conditions other than bronchospasm. Selective and discrete adaptation to bronchospasm may not be neurally possible. The effective adaptation to anaphylactic stress, then, would be a general dampening or lack of activation of facilitatory processes. Conversely, a general augmentation in this area of sensory input may be necessary for the nervous system normally to elaborate air-searching behavior. We would, therefore, suggest that the activity of the midbrain reticulum is intrinsically involved in the processes which direct organismic adaptation toward internal or external sources of danger. If the overactivity of this area is involved in the conversion of a primitive body defense to a lethal syndrome, then the level of activity of the midbrain with respect to vital, life-saving reflexes bears further investigation.

Whatever specific mechanisms were involved, augmentation of both afferent and efferent central response to allergenic bronchospasm and development of the excited phase of the allergic reaction were diminished by the lesion. Somewhat to our surprise, the animals were not asleep, perhaps because the lesion was not extensive; in fact, they were normally excited by cardiac puncture but calm during brochospasm. Between the behavioral extremes of deep sleep and excitement there appears to be an optimal neurophysiologic range within which neural systems can inhibit excited, externally directed, and maladaptive response to bronchospasm. The effect of the lesion may have been to contain brain stem function within this optimal range, characterized by inhibition of both peripheral reactivity and a cycle of central events.

The results lead us to the view that in the susceptible allergic patient there is a heightened readiness of midbrain systems to elaborate a response. We would think that the action of sedative drugs, emotions, and metabolic agents [15] in the presence of allergenic bronchospasm may be related to an interacting effect on the function and reactivity of the midbrain reticulum.

Summary

To test the notion that the central nervous system is involved in the course and sequence of anaphylaxis, lesions were placed in the brain stem of 17 sensitized guinea pigs.

Anaphylaxis was observed to involve maladaptive behavior, the animal excitedly responding to an internal stimulus of bronchospasm as though he were externally deprived of air. We observed an initial phase, of tracheobronchial irritation, and a second, lethal phase, of hyperpnea, excitement, and air searching.

Bilaterally symmetrical lesions in the midbrain reticulum at the level of the superior colliculus inhibited anaphylaxis and abolished the facilitation of expiratory secretory and motor mechanisms of the second phase, similar results were obtained with a lesion interrupting portions of medullary reticulum.

A review of related pathophysiologic mechanisms indicates that augmentation and diminution of both afferent and efferent central response to allergenic bronchospasm is related to the function of the midbrain.

The relationship of the area to processes directing adaptation toward the internal or external milieu and to the function of regulatory mechanisms is noted, and it is surmised that a heightened readiness for response of midbrain mechanisms may characterize the allergic person.

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Effect of Cortisone upon Spinal Cord Regeneration in Adult Rat

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Despite recent advances in caring for the neurologically crippled patient, there has been little progress in preventing permanent loss of function when tissue of the central nervous system is severely injured. The problem remains one of a lack of regeneration when central nerve fibers are completely destroyed. The present investigation was undertaken to determine whether cortisone would have a favorable influence upon the healing of a completely severed spinal cord.

Although not commonly recognized, there appears to be a natural inclination for the regeneration of severed central nerve fibers. This observation was first made by Ramón y Cajal,[1] who described an abortive growth of these structures after severance, the fibers appearing to be blocked in their growth by the formation of a fibrous and glial tissue barrier at the site of injury.

Windle, Clemente, Scott, and Chambers [2] reported histologic and electrophysiologic evidence of intraspinal regeneration following complete transection of the cord in the cat, provided the bacterial polysaccharide Piromen (derived from pseudomonas aeruginosa) was administered to the animal. These authors indicated that the success of their experiments was due to the inhibition of development of the pia-glial scar by the polysaccharide. Failure of benefit to the human with spinal cord injury by Piromen was reported by Friedlander and Bailey.[3]

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However, the experimental demonstration of favorable influence on central nervous system regeneration by the use of this substance has stimulated considerable interest in the problem and has introduced the possibility that other drugs with a similar action might also exert a favorable influence on central nerve regeneration.

In 1950 [4] Ragan and his associates demonstrated the inhibition by cortisone of new connective tissue growth in wounds of the rabbit. From the same laboratory in 1953 [5] it was reported that a similar delay in healing occurred in the rat, but a lag period of one-half to four days was noted. A study of the effect of this hormone on the healing of central nervous system wounds in the dog was made by Boldrey, Giansiracusa, and Beltran in 1951 [6]; these observers estimated that there was 20% to 50% inhibition of gliosis in the cortex and white matter of the dog brain.

These investigations pointed toward an inhibitory effect of cortisone on both the fibrous and the glial tissue of the scar thought to block the new growth of nerve fibers in the central nervous system. For that reason it was proposed that cortisone should exert a favorable influence upon regeneration of central neurons.

In presenting the results of studies of the effect of Piromen upon central nervous tissue regeneration, Windle and his co-workers [2] reported that preliminary observations on four cats given corticotropin indicated a response similar to that of Piromen. Wolf,[2] in discussing the above paper, stated that his studies on cortisone administration to rats with spinal cord lesions had not produced any favorable results. Windle,

Clemente, and Chambers,[7] in an addendum to another paper reporting their Piromen studies, noted that corticotropin administration to two cats for 36 days and one rabbit for 46 days gave results similar to those obtained by the use of Piromen; cortisone treatment of two rabbits for 35 days showed no evidence of inhibition of the scar at the site of injury. However, only 10 mg. of cortisone daily was given these animals. In the absence of a conclusive report on the influence of cortisone upon central nervous system regeneration, the present investigation was begun.

Material and Methods

Forty-eight albino rats (Rolfsmeyer) were used for these experiments, the animals weighing between 100 and 250 gm. at the beginning of the study. Female rats were chosen because of the easier bladder care in that sex. Rockland mouse diet and tap water were supplied ad libitum throughout the experiment. Thirty-two other rats were used in preliminary experiments to determine dosage, technique of operation, and postsurgical care.

One-half of the rats were treated with intramuscular injections of cortisone acetate, 0.06 mg. per gram of body weight initially, the amount being changed to 0.03 mg. per gram of body weight, or the medication stopped completely, when the animal appeared to be unable to tolerate more. The remaining animals were given the solution used for suspending the cortisone in an amount equal by volume to that given the rats in the treated group. This suspending solution was 0.9% benzyl alcohol, 0.9% sodium chloride, 0.4% polysorbate 80 U. S. P. (polyoxyethylene [20] sorbitan mono-oleate), 0.5% sodium carboxymethylcellulose, and 97.3% purified water U. S. P.

On the fourth day of treatment a middorsal spinal cord transection was made in each animal with a sharp knife after first picking up the spinal cord with a small hook. Great care was taken to cut all fibers at that level. The spinal cords were not sutured together after the transection. It was necessary to empty the bladders manually three times a day until automatic emptying of the bladders occurred two to four weeks postoperatively. The wire bottoms of the cages were covered with cardboard to protect the extremities and tails of the animals.

The period of observation and treatment with cortisone in each animal that survived for 14 or more days following the cord transection is indicated in the accompanying Table. The longest period of observation in any animal was 142 days; the longest period that any rat received cortisone was 38 days. Of the 20 animals surviving the transection for 14 or more days, 6 received cortisone. Seven of the rats were killed; six of these were control rats killed to provide appropriate controls for treated animals, and one was a treated rat killed at the termination of the experiment.

Rats Surviving Spinal Cord Transection Fourteen Days Or Longer

Survival Time, Days	Cortisone Administration, Days	
	0.6 Mg. per Gm. Wt.	0.03 Mg. per Gm. Wt.
142	0	0
132	6	8
132	13	0
111	0	0
98	0	0
87	0	0
80	0	0
79	0	0
59	0	0
59	0	0
35	0	0
32	10	20
31	0	0
30	13	25
29	0	0
23	27	0
17	0	0
16	0	0
14	8	10
14	10	7

When the rats died or were killed, the entire spinal column was excised and fixed in 10% formalin. After fixation the spinal columns and attached fragments of muscle were dissected from the spinal cord. Two-centimeter segments of the cords, including the transected areas, were then placed in 10% formalin and were embedded in paraffin. Alternate longitudinal sections were stained for study of connective tissue by Gomori's trichrome method, for study of nerve fibers by the Holmes technique, and for general survey by hematoxylin and eosin preparation. Microscopic examinations were made of the spinal cords from all rats surviving more than two days, with the exception of two animals inadvertently omitted, which lived for five and six days, respectively, after the operation. In all instances in which union of the two ends of the spinal cord occurred, semiserial sections were made through the areas of injury; these were stained as indicated above.

Results

All animals were observed for functional evidence of regeneration from the time they were operated upon until they died or were killed. Spinal reflexes were confusing in the evaluation of the rats' central nervous system, and true motor activity was re-

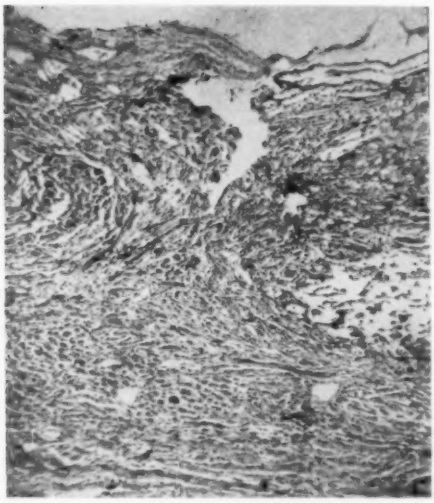


Fig. 1.—Typical scar at the site of spinal cord transection. Dense, irregularly arranged connective tissue forms an apparent barrier to the growth of nerve fibers. The period of observation of this animal was 132 days after spinal cord transection. Masson stain; × 110.

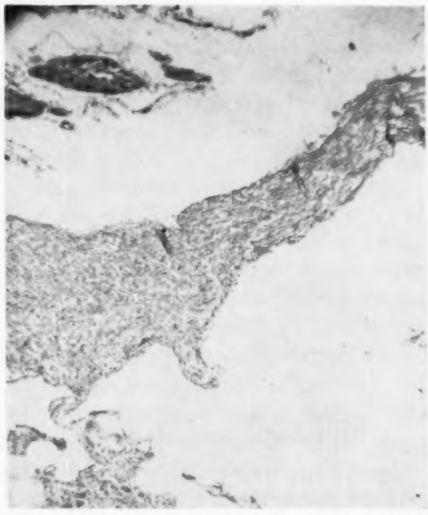


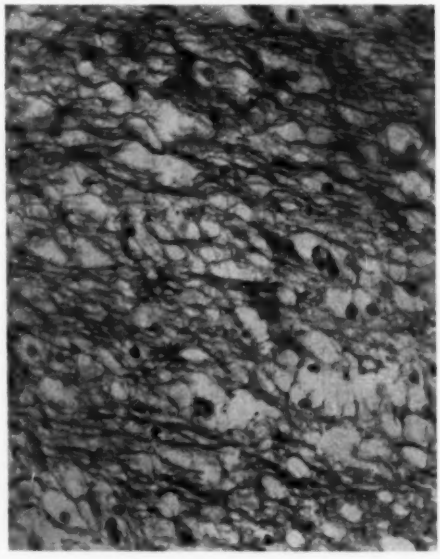
Fig. 2.—Band of nerve fibers at the site of cord transection in the control animal that regained function. There is minimal distortion by scar tissue. Holmes stain; × 110.

gained in only one of the animals, a rat from the control group. On the 33d postoperative day this animal was noted to move the right hindleg and to be sensitive to the injection of the suspending solution in that area. Gradually the posterior extremities began functioning more and the animal was able to stand on its hindlegs.

A study of the connective tissue deposition at the site of injury to the spinal cords showed that the amount of this material depended somewhat upon the duration of the postoperative survival, but there was no difference between the control animals and the cortisone-treated animals. The development of the scar is illustrated in Figure 1. Although special stains for glial tissue were not made, this type of connective tissue appeared to be a significant proportion of the scar matrix but did not differ in amount of development in the control animals as compared with the treated animals.

Nerve fibers spanning the site of transection were seen in the spinal cord of only one rat, the animal previously described as having regained some function. This band of nerve fibers is shown in Figures 2 and 3. These fibers could be followed very clearly into the adjacent spinal cord on each side; they were without significant scar tissue and so perfectly preserved that the observer

Fig. 3.—Greater magnification of nerve fibers described in Figure 2. Holmes stain; × 950.



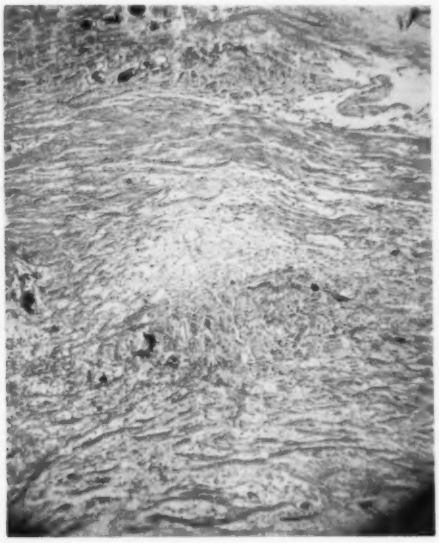


Fig. 4.—Bundle of nerve fibers ending in scar at the place of transection of the spinal cord. Holmes stain; × 110.

would conclude that this small band of fibers was not cut at the time of the spinal cord transection.

In the other spinal cords studied nerve fibers could be seen ending in the scar adjacent to the site of transection (Fig. 4). In no instance did these nerve fibers continue across the site of section of the cord.

A confusing aspect of the histologic observations was the presence of nerve fibers (Fig. 5) from the adjacent peripheral nerve roots growing into the scar, and even across the scarred area of the cord. Careful observation of semiserial sections was necessary to conclude that these fibers were actually arising from outside the spinal cord proper.

Comment

As indicated above, early histologic observations were not emphasized in these animals, and therefore one cannot conclude that there was no temporary inhibition of fibrosis or gliosis in the treated animals. However, the late stages seem to be of most importance concerning the central nerve regeneration problem, and attention was focused upon that aspect of the problem.

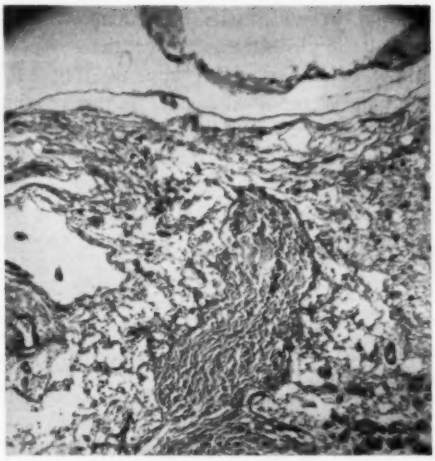


Fig. 5.—Bundle of nerve fibers at the point of spinal cord transection, shown by semiserial section to be coming in from outside the spinal cord proper. Holmes stain; × 110.

The presence of a band of intact nerve fibers across the site of transection in the one animal which regained some function was most likely due to the fact that the spinal cord was not completely severed, despite meticulous care in cutting the cord in each animal. It is believed that the possibility of such an error in technique should be considered in the evaluation of any past or future experiments of this nature.

The presence of nerve fibers in the scar and across the transected area originating from the roots of peripheral nerves can be a point of confusion in interpreting histologic studies. However, these experiments demonstrated that with semiserial sections one can trace the origin of these nerve fibers to the peripheral nerve tissue. Therefore the simple presence of definite nerve fibers across a point of transection of the spinal cord does not mean that these fibers are regenerating central neurons.

Summary

Observations are recorded upon 48 female albino rats studied for varying periods of time following middorsal spinal cord transection, one-half of the rats receiving cortisone and one-half of them receiving the

material in which the cortisone was suspended for injection. Other than in one animal in the control group, no return of function is reported; it is concluded that this rat had an incomplete transection of the cord due to error in technique. A lack of histologic evidence of central neuron regeneration is presented, and no difference between the treated and the untreated animals in the development of connective tissue is shown.

Emma Gene Forsythe and Carolyn Anderson gave technical assistance. Photographs were made by John Dickson.

University of Mississippi Medical Center (6).

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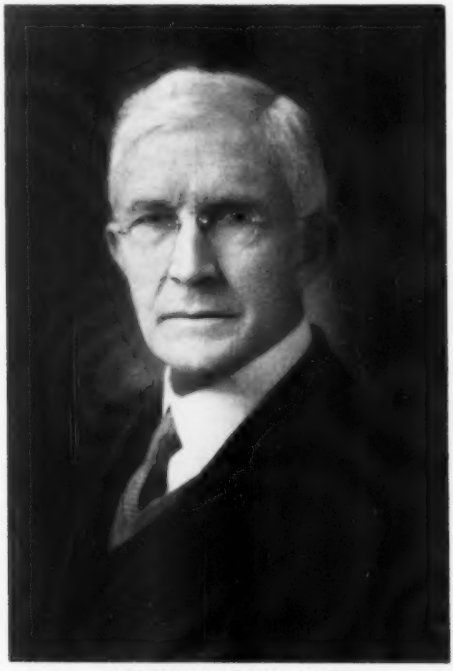
Obituaries

ANDREW H. WOODS, M.D.

1872-1956

Andrew H. Woods died in the Newton-Wellesley Hospital, Newton, Mass., on Nov. 5, 1956, the result of injuries suffered when struck by an automobile a month earlier. Andrew Woods was born on Aug. 25, 1872, in Hartwood, Va., the son of a Presbyterian minister. His school life away from home began in 1886 at Pantops Academy, in Charlottesville; in 1890 he enrolled in Washington and Lee University. He received the bachelor's degree at the end of his third year, and two years of teaching followed. In 1895, he won a four-year scholarship in the Department of Medicine of the University of Pennsylvania. In 1899 he sacrificed an appointment as intern at the University to accept an invitation to help in reorganizing the Chinese school later to be known as "Canton Christian College," with a view to founding its medical department.

This service was carried on for eight years in the face of disturbances connected with the Boxer movement. In 1907 Dr. Woods, his wife, and first son returned to the United States, where he began medical practice in Bryn Mawr.



ANDREW WOODS, M.D.

1872-1956

Here he atoned for the hospital experience missed in 1899 by spending his afternoons under Dr. Spiller in the clinics and wards of the Philadelphia General Hospital as assistant neurologist, with teaching duties.

Like many distinguished neurologists, Dr. Woods in his more mature years became interested in psychiatry, and this interest impressed deeply his professional life throughout his service in World War I and the following years, until his retirement in 1941.

When, in 1919, the Rockefeller Foundation recruited the faculty for the new Peking Union Medical College, they persuaded Dr. Woods to head the Department of Neurology. He found the organization "ideal—possessed of every facility for clinical work and research." The institution was judged at that time "the finest medical school plant in the world, with a faculty of top-ranking scientists from Europe, Britain, and America." Dr. Woods was responsible for the teaching of psychiatry as well as neurology, and left a record of inspiring standards in instruction of his Chinese students in the classroom and hospital wards. The Trustees' minute marking Dr. Woods' resignation in 1928 paid tribute to his success in these functions, and in arousing "interest among the governing classes of China in the proper care of mental disease."

On his return to the United States, Dr. Woods met an invitation to take charge of the Iowa State Psychopathic Hospital and of the Department of Psychiatry in the University of Iowa. After spending the fall and early winter of 1928 with Dr. C. MacFie Campbell, head of the Boston Psychopathic Hospital, he assumed the post in Iowa City. A colleague comments that his "soundness of approach to the teaching of Psychiatry became immediately evident not only in the undergraduate classroom but also in graduate education as indicated by the high caliber of young men who came to study under his direction, many of whom later became heads of departments in other institutions. Under his guidance also there developed a new concept of mental disease and its problems in the legal profession and particularly the judiciary."

A bibliography of more than fifty titles bears witness to Dr. Woods' ability as a writer in his field, and to the success with which he carried the responsibility for making available the fruits of his rich experience. His participation in professional organizations included the vice-presidency of the American Neurological Association and long membership on the examining committee of the American Psychiatric Association.

KALMAN SANTHA, M.D.

1903-1956

Neurology has lost a leader and Hungary a brilliant clinician and teacher in the death of Kálmán Sántha on Dec. 6, 1956. He was professor of neurology in Debrecen, where Benedik had preceded him. He was a man of keen mind, loyal to his country, and devoted to research and scholarship. Like many others, however, his fortunes varied with the changes in the political wind, but the man was steadfast in the face of danger.

Because of frank expression of his independent opinions, he was expelled from the Hungarian Academy of Sciences and from his chair of neurology in the ancient University of Debrecen in 1951. He continued his work, however, as chief of a department of psychiatry and neurology in a country hospital.

As a young man of 33, he had come to the Montreal Neurological Institute in 1936 on a Rockefeller Fellowship. Even at that age, he already had a publication list of 26 items, on various neurological diseases, neurohistology, and neurological symptomatology and on "brain and intelligence."

In Canada he did outstanding work on cerebral circulation in the normal and epileptic brain. Later he contributed important studies on aphasia, the protruded intervertebral disk, hereditary diseases, and neuropathology.

Sántha was a professor in the highest tradition of scholarship, the acknowledged master of a school of younger neurologists in his fatherland. In addition to his professorship of neurology and psychiatry, he actually found time to inaugurate neurosurgery in his country, following, in that regard, the example of Otfried Foerster at Breslau.

His last frank letter to me was written in 1939, when the gloomy clouds of world war darkened the international sky. "You can imagine," he wrote, "the psychical influence of the ever-changing international situation. . . . Now . . . at least we are facing it a little more philosophically."

At last the pressure of rising public opinion in his country led to his reinstatement in the Academy of Sciences and in his professorship. But this came too late, alas, for the news reached him when the last days of a fatal illness were drawing to a close. And so only his dead body was carried back to his beloved Debrecen, where he was mourned by loyal disciples.

WILDER PENFIELD, M.D.

Books

BOOK REVIEWS

An Atlas of Muscle Pathology in Neuromuscular Disease. By J. Godwin Greenfield, M.D.; G. Milton Shy, M.D.; Ellsworth C. Alvord, M.D., and Leonard Berg, M.D. Price, $9.00. Pp. 116, with 93 figures, 48 in color. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1957.

The authors in their preface state that in developing this book they have tried to answer the questions: "What are the fundamental reactions of muscle to disease?" and "With what clinical entities are these reactions associated?" The first two-thirds of the book is devoted to the first question. With a series of superbly clear illustrations and a brief account in the text they have admirably and tersely fulfilled their intent. They divide the fundamental changes in muscle in response to disease into ten different categories, including structural changes in the muscle fiber, changes in muscle nuclei, changes in fiber size, ringed fibers, sarcoplasmic masses, changes in interstitial tissue, leukocyte infiltration, changes in muscle spindles and peripheral muscular nerves, the presence of basophilic fibers, and the pattern of the lesion.

In the last third of the book the authors set forth their clinical classification of neuromuscular diseases. There have been many such classifications, but this one seems to have an advantage in that it is simple and avoids the usual eponyms and terms of variable definition. This classification includes distal muscular syndromes, myotonic syndromes, proximal muscular syndromes, and myasthenia gravis. The authors outline the usual microscopic findings in these various categories and point out the considerable overlap in the microscopic picture and the absence of any clearly limited histological picture to any one syndrome.

This book is certainly a needed addition to the literature on muscle and will be appreciated by all who experience the difficulties of categorizing muscle diseases, either histologically or clinically.

FLETCHER MCDOWELL, M.D.

Autonomic Nervous System. W. S. Feldberg, Scientific Editor. (Brit. M. Bull. 13:153-228, 1957.) Price, $3.65. Pp. 77. The Medical Department, The British Council, 65 Davies St., London, W. 1, 1957.

This issue of the *British Medical Bulletin* is concerned with recent advances in knowledge about the autonomic nervous system, but it includes a wide range of pharmacological, anatomical, and physiological studies, some only distantly related to the autonomic system narrowly defined. Each of the authors is an active investigator of the aspect with which he is concerned. H. Blaschko writes on "Formation of Catechol Amines in the Animal Body"; Marthe Vogt, on "Sympathomimetic Amines in the Central Nervous System," and J. H. Burn, on "Acetylcholine and Cardiac Fibrillation." "The Intermediate Sympathetic Ganglia," by Professor Boyd, and "Collateral Sprouting in Response to Injury in the Autonomic Nervous System, and Its Consequences," by Drs. J. G. Murray and J. W. Thompson, are of direct relevance to the bedside problems of the clinician. Drs. S. M. Hilton and G. P. Lewis report the formation of a polypeptide vasodilator substance as a side-effect of a primary metabolic response to neural stimulation which may be of far-reaching significance. The other distinguished authors maintain the high level of these papers. Excellent planning and editing are evidenced throughout. The volume is concise and filled with new facts and formulations. While not an encyclopedic treatment of the subject, nevertheless it presents an adequate cross section of the contemporary scene as regards these problems. It is a highly polished gem that can be recommended with enthusiasm.

L. CHAPMAN, Ph.D.

An Analysis of Methods for Teaching Psychotherapy with Description of a New Approach

JOAN FLEMING, M.D., and DAVID A. HAMBURG, M.D., Chicago

Psychotherapy is essentially a process of communication. The student of psychotherapy needs first to learn how to perceive and interpret signals from his patient and from himself in forms differing from conventional communication. In our culture we utilize explicit verbal and behavioral expressions and hide or ignore the more affective personal signals. In most social situations, this mode of communication is adequate and is condoned as appropriate, but for the psychotherapist much more is necessary. He must be able to receive messages from his patient and himself, which arise from beneath the surface of their social façades.

Skill in psychotherapeutic communication depends upon development of the following capacities:

1. The recognition of the existence of nonverbal signals within behavior, and the capacity to accept their messages within the span of his own consciousness.

2. The ability to understand the meaning of these nonverbal, as well as the usual verbal, cues.

3. The capacity to observe and appreciate the meaning and appropriateness of his own reactions and responses to the patient's messages, thereby becoming a sensitive instrument for recording and understanding what is happening within and between the patient and himself.

4. The recognition of lacunae or distortions in the patient's communication. This is an important skill, for these indicate messages that are often most significant for the therapeutic process. They reveal a need in the patient for hiding, avoiding, or not knowing something. These distortions are resistances against full awareness, and the forms they take are valuable guides for diagnosis and understanding of the level and type of conflict in the patient.

5. Learning by the therapist, through experience, to estimate how much the patient is conscious of his signals and their messages and how much he is aware of the implicit meaning of what he says and does. These are the measures not only of insight but also of the patient's receptivity for therapeutic interpretation.

6. The capacity to understand the meaning of the patient's communications. This is a large part of the task of the therapist. Placing them together in an organized manner gives comprehensive meaning to the patient's problems and facilitates a diagnostic formulation. Skill in understanding is basic to the development of correct therapeutic responses to the patient.

7. Selection of responses appropriate to the therapeutic goal and in tune with the patient's receptivity at the time. This is the

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From the Institute for Psychosomatic and Psychiatric Research and Training of the Michael Reese Hospital.

crucial skill of the psychotherapist and determines the rate and course of progress in therapy.

8. Recognition of the effect of his interventions. This depends on understanding the patient's response to them and is an essential part of the therapist's task. Often the response is different from what was anticipated, and skill in determining the explanation for this discrepancy leads to deeper understanding of the patient's problem.

In summary, the skills needed to become a psychotherapist are (1) recognition and understanding of nonverbal signals, as well as the usual verbal cues; (2) self-observation and understanding of his own responses to the patient's behavior; (3) recognition of the distortions in the patient's communications; (4) estimation of resistance to insight; (5) selection of therapeutic responses appropriate to the level of insight and resistance manifested by the patient; (6) awareness and understanding of the effect of therapeutic interventions.

With these skills in mind, we examined and evaluated some of the methods utilized for teaching them to psychiatric residents. Special attention was directed to the case conference, since this is a common method in practice for many years, in which theoretical concepts of normal and abnormal behavior can be presented by demonstrations to augment formal lectures. The case conference has also been used to demonstrate the principles of therapeutic technique in specific behaviorial contexts. Although the best method for teaching psychotherapeutic skills is individual supervision, the case conference is more economical of time and provides contact with a wider variety of clinical material for a larger number of students. Details of behavior and technique can be better studied in supervision, but the case conference adds a larger perspective of time in summary form, which is often impossible in the supervisory setting.

One advantage offered by the case conference is the opportunity for the group to experience the processes of diagnostic thinking and therapeutic interpretation without the pressure of responsibility for therapeutic results inherent in the relationship with the actual patient. Relief from this responsibility permits a freer and more objective "laboratory" investigation of various factors in the therapeutic process and allows the members of the class to exercise their diagnostic and therapeutic skills in "trial action."

Exercise of observational powers and trial interpretation of data, available to all members of the class, constitutes the chief value of the case conference method for teaching psychotherapy. Being face to face with a patient in need of help carries pressures for immediate responses from the therapist, especially for the beginner, whose skills in self-observation and capacity for empathic identification are usually limited. More leisurely attention to his own associations and responses and the weighing of the possible meanings of the interactions between patient and doctor are valuable practice experiences in learning psychotherapy.

In evaluating the conventional method of presenting material in summarized reports of past therapeutic interviews by the therapist, we felt dissatisfied with the kind of clinical data available to the class. We then asked ourselves: What kind of clinical material best provides opportunities to learn the therapeutic skills that we have enumerated above?

First, we must have information about the patient. In general, the more immediate, alive, vivid and affect-full the reporting the closer will it approximate the primary therapeutic situation. Accuracy in painting a clear picture of the patient is of the greatest importance. Data on nonverbal behavior are essential; otherwise the nuances of tension and the peripheral cues to hidden meanings will be lost.

Second, we need to know a great deal about the doctor-patient relationship and interaction from the frame of reference of the therapist. He should supply the class with information on what cues from the

patient he perceived, how these stimulated his own thinking patterns, and what motivated him to respond as he did.

Third, we must know something about the sequence of stimulus and response in the reciprocal relationship between doctor and patient, indicating the movement of communication between them over time. It is the specific interplay of the two personalities in transaction and the context in which it occurs that teaches us most about the what, how, and why of psychotherapy and opens the way to the fullest understanding of the therapeutic process.

The following methods of presenting clinical material have been used under various circumstances: (*a*) playing a tape recording of an interview; (*b*) interviewing a patient in front of the class; (*c*) watching a psychotherapeutic session through a one-way vision screen, and (*d*) the traditional reporting in summary of past interviews conducted by the therapist. Before discussing our own method, we propose to review the advantages and disadvantages of the usual technique. Because they differ considerably in their strong and their weak points, it seems that the utilization of a variety of methods might be advantageous. The teacher who confines himself to only one method of presenting clinical data in teaching psychotherapy may be building a systematic source of error into his procedure. If he varies his approach, one method may succeed where another falls short, but the sum total of learning becomes broader and more complete. Even though considerable overlapping will result by combining the various methods, the teacher is still the primary agent in all of them for focusing the goals of learning. Certainly, there is much to recommend a more varied approach to the teaching of psychotherapy than has ordinarily been followed in many residency programs.

Certain factors in the class situation may facilitate or obstruct conditions most advantageous for learning psychotherapy.

1. The amount of time given to the class meeting is of great importance. Very often a large proportion of time is taken up in presenting the material, so that there is little opportunity for discussion of what the group observed, how they interpreted it, and their thoughts on possible technical interventions. The recognition of the place of the observed example in the larger range of pathology, nosology, and technique cannot receive attention if only a few minutes of class time remains. Postponement of the topics for discussion until the next meeting is not usually satisfactory, since the elapsed time dulls the memory of what had transpired. The time required depends to a large extent on the method of presenting the data and on the teaching aims of the instructor. If we compare different methods according to the time required, the following factors must be considered: A tape-recorded interview requires as much time to reproduce as was spent with the patient. If the interview lasted 45 minutes, half of a 90-minute class session is consumed in this task. An interview of a patient in front of the class can be shortened or lengthened, but often needs 45-60 minutes. Observation through a one-way-vision screen is not of much value unless the class remains until the interview is over. These three methods deal with the interview as it actually happened, although the closeness of the patient to the class varies. The conventional method, in which the student-therapist summarizes the interviews, may take more or less of class time, depending on the number of interviews he wishes to cover, the detail desired for class use, and the capacity of the student to select what is pertinent.

2. One must also take into account the impact of the class situation on the patient and the therapist. If the conventional method of reporting interviews is compared with the other three, a rough, but not universal, generalization emerges which brings out an important general difference between two basically different approaches to the teaching of psychotherapy. The conventional method might be designated as a "private" method; the other three, as "semi-

public" methods. The first is private in the sense that no one else has access to the interactions between therapist and patient. What goes on is strictly between them, and any information which others have is entirely secondhand. The remaining three methods are semipublic in the sense that in one way or another a third party has direct access to the interchange.

The principal advantage and limitation of the private method may be summarized in the phrase "spontaneous but distorted." Similarly, the principal advantage and limitation of the semipublic methods may be embodied in the phrase "accurate but constrained." Privacy contributes to a sense of security, which significantly affects both the participants. The patient is communicating with a person he presumably can trust and deals with that person alone for purposes solely to his own advantage. The same consideration applies to the therapist in the private situation. He is not in any direct way being judged by his peers or by those whose decisions may have an important influence on the subsequent course of his career. To protect his self-esteem and his own long-range interests as he perceives them, he may, if necessary, describe the therapeutic interaction, retrospectively, in terms that are favorable to himself. This selective coloring of the material is usually unconscious and beyond the control of the therapist. Thus, the therapist's sense of security in private situation provides us with a paradox; on the one hand, it enhances his personal comfort, so that he may be more spontaneous and "human" with the patient, two qualities that have much to do with producing desirable therapeutic results. On the other hand, this very security produces undesirable results from the teaching point of view, namely, the opportunity for selective distortion in subsequent reporting of the process. From the standpoint of the student, it may be worth while for him to sacrifice some degree of spontaneity and comfort in order to have a more effective learning experience. The sacrifice should ensure, in the long run, a more spontaneous and more technically adequate psychotherapeutic skill.

In this connection, it seems clear that the semipublic methods give a much more accurate representation of the actual interaction between therapist and patient. They provide a more realistic base for teaching psychotherapy. Still, the price we pay for this vividness may be fairly high. There is almost always some element of constraint and anxiety in the semipublic method. Thus, the raw material upon which we base our teaching is not the perfectly accurate representation of ordinary therapeutic interaction. It may be quite tense or wooden or excessively conventional. Time may be wasted in pointing out to a student his nontherapeutic behavior, which would not ordinarily have occurred if he were not being directly observed.

3. Another extremely important factor to consider in the comparison of different methods is the opportunity for class discussion. In the exchange between teacher and students observational powers are tested, questions are clarified, theoretical knowledge is integrated with clinical behavior, and diagnostic and therapeutic interpretations are practiced. The ease with which discussion can take place varies with the method employed. When a patient is interviewed in front of the group, class participation must usually be silent until the patient leaves the room. Otherwise, the trauma to the patient would be too great. In the conventional summarized report questions may be raised at any time by class or teacher. These questions are often valuable indications of the thinking of the questioner and require that gaps in information be provided by the reporter. There is, then, the disadvantage that much discussion time may be spent in filling in gaps before integration of observation and interpretation can occur. The chance for distortion or withholding of facts often requires much clarification of data before discussion can be more than vague speculation. The need

to remember and to condense diminishes the dramatic vividness of the therapeutic interaction and tends to lower the interest of the class, which is so far removed from active participation in the actual event. A tape recording gives a fuller account and can be interrupted for teaching purposes. The chief disadvantage here is the mechanical one. Both recording and playing back require special equipment and conditions. The one-way screen method permits no interruption of the interview for discussion of questions raised at a special moment. This may not be too great a disadvantage, provided discussion can be carried on immediately after the interview.

To summarize the problem of class discussion, the choice of method requires consideration of the total amount of time available, the quantity of information the class must remember before clarification and study can take place, and the ease with which small amounts of data can be examined in detail.

4. Another asset in the teaching of psychotherapy is the opportunity for validation of trial diagnoses and interpretations, which are important aspects of the learning experience of the class. Without a chance to hear the outcome of the actual therapy, the class discussion may degenerate into speculation only. Consequently, early diagnostic formulations and suggested technical maneuvers need to be checked against what actually happened in the course of therapy. In continuous case conferences this condition is well satisfied, since the ongoing reports can confirm or deny the tentative interpretations by the class at any time. Class suggestions may even have an effect on the outcome if the therapist makes use of them with the patient. The conventional method of having a different student present a case at each class meeting makes is difficult to follow up the results of therapy. However, when the student covers a large block of therapeutic sessions in one class meeting, some validation can be accomplished by interrupting the presentation for discussion, which can be checked subsequently. A tape recording provides some opportunity for validation if the playing is interrupted for suggestions and predictions and then continued. There is usually time for only one taped interview in one class session, and the long-range perspective on the therapeutic process must be sacrificed. Validation when the one-way screen method is used is almost absent unless repeated observations of the same patient are possible. Interview of the patient in front of the class is usually done for diagnostic evaluation only. Subsequent events might be reported at another time to provide the opportunity for perspective and validation.

5. Variety of clinical illustration has already been mentioned as one advantage of the case conference over individual supervision. If the continuing process is a teaching goal, variety must take second place because of the time necessarily consumed by continuous reports, tape recordings, and observations through a one-way vision screen. Not as many patients can be studied, and a variety of pathology and the range of specific problem situations will be less. These methods have the advantage of more detailed study of therapeutic process and of follow-up on results. The conventional summarized report can meet the wish for variety with sacrifice of detail. The diagnostic interview in front of the class offers the chance for large variety and detailed study of each interview, but little validation of the therapeutic process.

Another type of learning experience valuable in preparation for postresidency practice is the problem situation. This includes not just pathology, nosology, and general technique but also an evaluation of environmental and social factors involved in the patient's referral and treatment. A case conference setting can be used to present a variety of problem situations which the resident will undoubtedly meet in his later practice but for which he is often unprepared by his residency training. We refer here to situations such as consultation on a patient in a general hospital, feasibility of

outpatient therapy for out-of-town patients, special questions dependent on the means of referral, problems arising when the patient has seen other psychotherapists, the various aspects of fee-setting, interviews with relatives in office practice, etc. The conventional reporting and taped interviews seem to be the most flexible methods of presenting data focusing on such problem situations.

It seems clear that the important goals of a case conference cannot entirely be reached by lectures on psychotherapy. The case conference will continue to have its own distinctive place in the training of psychotherapists. Yet the presence of a case conference in the curriculum, even with a good teacher, does not in itself guarantee that these goals will be reached. Having used various approaches in our own teaching, and having reviewed the advantages and limitations of (1) the conventional case presentation, (2) an interview of a patient in the presence of the class, (3) a tape recording of a therapeutic interview, and (4) a one-way screen view of therapeutic interaction, we are left with the conclusion that there are still significant deficiencies in our repertoire of teaching devices for presenting clinical data.

In general, it would be very desirable to have a method which could achieve the following characteristics described above and reviewed here for emphasis: (1) make the full data of doctor-patient interaction available at first-hand to the students, including the therapist's participation and the nonverbal communication between the two participants; (2) make the therapist's thinking readily available at various important points in the course of the interview; (3) facilitate maximum participation of the class in thinking and discussion; (4) allow the impact of the therapist's intervention to be clearly understood by the class; (5) create a situation so structured that, following discussion by the class, and resumption of the interview, the therapist's modified technique and its effect on the patient can be observed; (6) economize on time, so that much interesting and informative material can be presented within a relatively short span and ample discussion permitted, and (7) avoid harm to the patient.

During the past five years we have developed and gained considerable experience with a method that goes a long way toward meeting these objectives, even though it has its own limitations, which we shall point out. Since we feel it represents a worth-while addition to the repertoire of available methods for clinical teaching, we now wish to describe it and will later present a verbatim detailed illustration with explanatory comments.

Description of the Dynamimetic Interview (DMI)

In this procedure, the imitation of an interview with a patient well known to the teacher supplies the data for observation and practice in psychotherapy. The teacher selects a patient from his practice and proceeds to "be this patient" in an interview with a resident who functions as the therapist, and who is instructed to behave as he would with any patient in a clinical interview. The biographical and therapeutic history of this real patient provides the basis for the behavior of the teacher-patient. The objective is to expose the story of the patient, with as faithful as possible a portrayal of his behavior patterns as revealed in his previous therapeutic relationship.

There is, however, no attempt to reproduce the original interviews which occurred between the patient and the therapist-teacher. This would be impossible, since it would involve the reproduction of a two-person experience. It would be possible to memorize a tape recording for such a dramatization, to be spoken by skilled actors; but this degree of reproduction of the original interview is not our objective. Rather, we attempt to provide characteristic patient material in a situation that is an authentic interview in itself. A reproductive staging would interfere with the "aliveness" of the participation by the student-therapist and

the class. A significant value of the dynamimetic interview is the demonstration to the class of the patient's reactions which are immediate and appropriate responses to the behavior of the therapist. Roughly speaking, the teacher-patient responds as the patient might have responded to this interview, not necessarily as the patient did respond to the original one.

By means of the DMI, the members of the class become participant observers of the interaction between the patient and the therapist. They can see what occurs in the immediate situation. First-hand information is available, which can be identified, described, explained, and interpreted as it is happening. Nonverbal cues can be observed in their verbal context. The sequence of stimulus and response in the series of therapeutic interactions is accessible for intensive study. By this method the raw data of psychodynamics, personality structure, interview technique, and the phenomena of the doctor-patient relationship become part of the immediate experience of the group and advantageous for the learning process.

To orient the student-therapist to the particular situation, as much identifying information is given to him as is necessary, namely, the name and age of the patient, the source of the referral, the reason for the referral, and the place in which the patient is being seen (hospital, clinic, office, home). The class period is 90 minutes. The usual pattern is as follows: interview; discussion; interview; discussion. As we have used the DMI, the interview segment lasts from 15 to 30 minutes, but this is a flexible feature of this device.

A number of variations of the procedure are possible, depending on the teaching objectives and other individualizing factors. 1. The interview can continue until the student-therapist terminates it. At this time, discussion of the process can take place without the delay or the condensation and selections which so frequently distort the report of a clinical interview. 2. The teacher who has participated in a double role during the DMI can choose a topic for discussion, and so direct the next step in learning, or this can be done by any member of the class. This part of the procedure is not different from the usual conventional case report. Here, however, the quality of immediacy and first-hand participation by the group sharpen their powers of observation and challenge their diagnostic ability.

This device offers several special opportunities for teaching and learning. First, the dramatic action can be stopped at any moment when special points of diagnosis, dynamics, or technique can be highlighted. Errors can be pinpointed as they occur and discussed constructively with a view toward correction. The interview can then be resumed; neglected areas can be explored, and different technical approaches tried. Observation is changed to discussion by shifting roles. The patient becomes a teacher; the therapist becomes a student, and the observers need no longer be silent onlookers. Such interruptions obviously cannot take place in an interview where a real patient is present.

A second special opportunity offered by this teaching device is the chance to study the diagnostic thinking of the therapist. During the interruptions or after the interview is over, the therapist can report his associations and the interpretations which he made to himself in the process of attempting to understand the patient and his illness. When the interview is interrupted with the question, "Why did you say that?" or, "Why in that way?" or, "Why that remark at this time?" the student-therapist is given an opportunity to catch his peripheral reactions and to make them more conscious, to clarify his half-formed thoughts, and to crystallize the reasons for his therapeutic interventions. If he were describing an interview or a tape recording held earlier with this patient, much of this process would probably be lost. We agree with Deutsch and Murphy [1] that "therapy can be learned only by doing, analyzing, and redoing." We have attempted with the DMI to produce a

teaching situation where opportunities for practice and redoing exist.

A third special value of the DMI is the opportunity to study the results produced by a given technical approach of the therapist. These results can be observed in the patient's explicit behavior, but, in addition, this "patient" in the role of teacher can report on unverbalized reactions to the therapist's behavior. For instance, the habit of staring at the patient with an intently penetrating glance or the use of a particular tone of voice is an example of habits of which the student is usually not aware. He is, therefore, not alert to their effect on the patient. These points lead to a discussion of the interfering influences raised by the emotional problems of the therapist. The subject of the counterreactions of the therapist is more appropriately taken up in other teaching situations, such as individual supervision; but in the DMI attention can be called to their existence and their effect in the immediate context.

We have paid considerable attention to possible limitations in the DMI, since we are well aware that every gain has its price. The final accounting as to the usefulness of any method must depend on an analysis of its advantages and its limitations. During the past several years, whenever one of us took the role of teacher-patient in a DMI session, the other served as observer. In this way, we attempted to get some perspective on the method, including its possible limitations. In addition, at the end of each academic year, we interviewed the residents in some detail on their assessment of the DMI. From them we were able to get a constructively critical analysis of the DMI from another vantage point. Furthermore, all of our DMI sessions were recorded on tape, and we have played back a number of these at a later date in order to study in detail the characteristics of this device. From all these various sources of observation, we have gradually arrived at our present assessment of the DMI, both as to its positive characteristics, which we have already outlined, and its possible limitations, which we will here discuss under four headings: (1) range of applicability, (2) emotional aspects, (3) similarity to a real interview, and (4) problems for the teacher.

1. When the DMI was first developed by one of us (J. F.), some psychiatrists raised the question whether a successful use of the device would be limited to its originator or, at any rate, to persons who were deeply interested in it and convinced of its merits. Another similar question was whether the method would require a highly skilled actor. In order to get a better idea of the reproducibility of the device, a second person (D. H.), who was initially interested but skeptical of the value of the DMI, took the role of teacher-patient in a series of sessions. In our judgment, and in the judgment of the residents who participated in the class sessions, the DMI sessions were on the whole quite useful regardless of which of us took the teacher-patient role. It is clear that the effectiveness of the device does not depend on its use by the originator, and, indeed, does not depend on the dedication of the teacher to it as a major teaching enterprise. Furthermore, the usefulness of our DMI session is particularly interesting in view of the fact that neither of us is a skillful actor. Perhaps the effectiveness of the DMI would be increased somewhat if the teacher were himself a skillful actor, but we have no experience from which to evaluate this possibility.

From what has already been said, it can be seen that it makes no difference whether the teacher is a man or a woman; the DMI can be used perfectly well in either case. However, there is a sex-linked limitation which should be mentioned. The teacher can only effectively present patients of his own sex. If, therefore, the teacher is a man, he must largely leave out considerations specific to the psychology and treatment of women, although he can bring these in to some extent during periods of class discussion. Even with this limitation, the teacher has such a broad field of psychodynamics, interview techniques, and psychotherapy

available to him that there is surely no shortage of teaching material.

Another important question on the range of this device is the issue of diagnosis *vs.* therapy. That is, does the DMI inherently address itself only to the diagnostic interview, or can it be extended to deal with the process of psychotherapy over an extended time period? There is little doubt that its primary usefulness is in dealing with the diagnostic interview. However, we have on several occasions carried out a series of interviews with the same teacher-patient, thus extending the DMI to deal with the opening phase of therapy. It seems to serve this purpose well; but we have so far not made any systematic attempt to use the DMI for teaching later phases of therapy. Such exploration remains for future work. As noted elsewhere, this method is flexible in its applicability to different learning problems and different stages of development of psychotherapeutic skills. The focus of the DMI may be set by the teacher in keeping with his specific goals, which, in turn, would vary with beginning and advanced students.

2. The crucial question here is whether there are emotional repercussions of the procedure which are likely to interfere with the learning process. The method does generate some tension in the class, particularly in the resident conducting the interview. Is the discomfort so great that it undermines the learning potentialities in the situation? Or, do the residents usually learn a great deal in spite of the tension? Is it simply the price we have to pay for the other advantages of the DMI? Is it possible that the tension may actually facilitate learning?

Before discussing these questions, it is appropriate to amplify the nature of the emotional experience. The residents who have conducted these interviews by and large find them tenser and more difficult than the conventional case presentation. The intensity of the discomfort varies a great deal from one resident to another, but all indicate that it is at least initially an uneasy experience. When the source of this discomfort is pursued, it usually turns out to be a fear of being exposed and humiliated. There is no way that the interviewer can hide his actual operations in this procedure. He cannot smooth them over, as he can in a conventional case presentation. He is often fearful that he will be criticized for his interviewing difficulties both by his classmates and, perhaps more importantly, by his teacher. This problem is particularly difficult for those residents who are highly competitive, feeling that they must make a better impression than the others have made, yet fearing that they will not be able to do so. The fear of criticism varies from time to time, diminishing for a while after a session in which the interviewer has done a particularly effective job, and increasing for a while after a session in which the interviewer has encountered gross difficulties.

From the standpoint of the class members who are not conducting the interview, there is little doubt that their anxiety is not great enough to interfere with the learning process, even though they sometimes feel quite uneasy through an empathic relation with their fellow resident who is, in a sense, "on the spot." As for the therapist himself, few residents have been so anxious that they were not able to learn something from the experience, and the majority felt that it was profitable in spite of low-grade anxiety.

In general, there is no reason to believe that learning proceeds only in totally comfortable situations. The newer approaches to clinical teaching, such as DMI, present a paradox: The main source of a resident's anxiety is also the factor of greatest constructive potentiality, namely, the impossibility of presenting a sugar-coated version of the interview. The very thing that the insecure student may wish to hide is often the thing he needs most to see—his actual participation in the therapeutic interaction. What the teacher can do to deal with this

problem constructively will be discussed later.

3. One question which arose early was whether or not we were trying to reproduce the actual interview with the original patient. Let us reiterate here that this is not our intent. The resident-therapist is not, after all, the original interviewer and usually does not pursue the original course. The response of the "class patient," like that of the original patient, is largely determined by the attitude and line of inquiry of the therapist.

A more important problem arises in the difficulty which the resident has in distinguishing between the teacher-as-teacher and the teacher-as-patient. He may, for instance, notice a frown at a certain point in the interview and be puzzled as to whether the teacher was attempting to portray the patient's feeling or simply experiencing some personal discomfort. More generally, the resident may wonder whether the personality characteristics in evidence are chiefly those of the patient or those of the teacher. The residents report that all the patients portrayed by a given teacher have considerable similarity, reflecting some basic characteristics of the teacher. There were, however, substantial differences between patients too. A further complicating factor is that the resident has a previously existing relationship with the teacher, and for some it is difficult to shift from this established pattern of interaction to a new one, appropriate to a therapist-patient relationship. All of these difficulties ease considerably with the passage of time and with repetition of the experience. Most residents develop a fairly clear base line of the teacher-as-teacher and learn to differentiate this from the behavior which is specific to a given patient. Furthermore, with practice in the DMI, most of them become skillful in shifting roles to become therapist during a class session.

Residents who participated in a series of DMI sessions over two years of their training were agreed that the resident-therapist is somewhat less spontaneous in this situation than he would be with an actual patient. Occasionally, anxiety and resentment over being "on the spot" may lead to major distortions in a resident's behavior; this is usually related to personal problems of a particular resident. But most of the residents expressed the view, in which we would concur, that therapeutic behavior is fundamentally consistent and, therefore, the therapist conducts the interview in much the same way as he would with an actual patient, except for some loss of spontaneity. In listening to the tape recordings of DMI sessions, we have been impressed with the great variety in the quality of interviewing done by different residents. We have checked this material against the available information from other sources, such as individual supervisors, and found impressive consistency. A resident who showed ability in interviewing in one setting usually showed it in the DMI as well. It does seem, however, that the emotional overtones of a therapeutic relationship are often minimal in the DMI, with a tendency toward formal, conventional behavior on the part of both therapist and patient. This is a factor which the teacher should take into account.

4. We have already pointed out that there are emotional problems in the use of the DMI. The teacher can do much to ease or intensify these problems, depending on his own behavior. How can the teacher help the resident to learn more and more about his own participation in the therapeutic interview without causing him unnecessary distress? In general, we feel that the teacher must strive for an atmosphere of frankness without attacking anyone. Criticism should be constructive. Neither teacher nor student should permit themselves self-aggrandizing comments at the expense of the therapist. Difficulties should be approached honestly and yet sympathetically. The teacher should be consistently alert to the fact that he sets the emotional climate for the class, and this climate, in turn, has a great bearing on

originality of thinking, freedom of expression, and the total learning experience.

In this connection, we feel that attention should be paid to the choice of resident to conduct each interview. In our experience, the class has consisted of second- and third-year residents. We have come increasingly to feel that it is wise to allow each resident a considerable period in the class before asking him to conduct a DMI. For one thing, this gives him opportunity to become familiar with the teacher's behavior and so makes it easier for him to differentiate the teacher's characteristics from those of a patient being portrayed. Furthermore, tension tends to ease with familiarity, and confidence grows with gradually increasing participation in the class discussions.

In addition to avoiding inexperienced residents, we try to avoid those who are currently undergoing a difficult period in their personal lives. An extremely tense, insecure resident who is easily threatened and highly vulnerable to criticism is not likely to conduct a fruitful DMI, and can better participate as a noninterviewing class member until he has made some progress with his personal problems.

Another problem for the teacher is that of switching roles from "patient" to teacher each time the interview is interrupted for class discussion. Indeed, at the same time the teacher is participating as patient, he is to some extent observing as teacher—for example, noting points which should be discussed with the class. This shifting, and even simultaneous, presence of two roles is a responsibility that is initially more difficult than conventional teaching. With time, however, skill develops; we have not found this double function a handicap after the first few sessions. While it does require greater concentration on the part of the teacher, we feel that it is well worth the effort because it can add so much to the class experience.

Transcript of a Recorded Interview Between the Teacher (as Patient) and a Resident (as Therapist), with Class Discussion

Preliminary

The following information was given to the therapist before he began to interview the patient:

The patient is Irish. Her name is Mrs. O'Reilly. She is 48 years old, married, and was referred by an internist, who made no prior contact with the psychiatrist.

Dynamimetic Interview

Doctor: How do you do, Mrs. O'Reilly? I am Dr. Bierle.

Patient: Good morning, Doctor. Dr. Bierle?

Doctor: That's right. I wonder if you could tell me something about why you decided to come to see me.

Patient: Well, I decided to come because my doctor—I have been seeing him for quite a while—. I have been having a lot of trouble in my stomach, and headaches and just feeling no good, and he looked me over and he said I was too fat, and I should reduce, but he told me I ought to come and talk to you, because you were a nerve doctor. He thinks it's my nerves. I think so, too. I am a nurse, or I was a nurse; so I know a little about some of these things, but I don't know what to do about them.

Doctor: How long have you been troubled?

Patient: Oh, I've had headaches for years, and stomach trouble off and on. It just gets to feeling like a great big lump, in my stomach, and lately, maybe in the last six months or so, I've lost a little appetite, but I haven't lost any weight.

Doctor: So it feels like a great big lump.

Patient: Yes, and when I do eat, it always makes me feel uncomfortable.

Doctor: Do you feel bloated?

Patient: Yes.

Doctor: Do you have any other symptoms with this?

Patient: Well, I belch a lot with it, but that's been going on I'd say, oh, off and on at times, I've had it, but now, ever since about last spring.

Doctor: Last spring. It's been constant since then?

Patient: Mmm.

Doctor: Previously you've had it for years, but off and on?

Patient: Off and on, yes. It would never last as long as this.

Doctor: Do you have pain also?

Patient: Well it's . . . it's not real pain. It's more like a pressure. It hurts, and it's sore when I press on it.

Doctor: Any one particular spot on your abdomen?

Patient: Just right up here—(cough). It kind of keeps me awake at night, too. At least I think that's what keeps me awake.

Doctor: You don't sleep well?

Patient: No.

Doctor: Does this awaken you, or do you have trouble getting . . .?

Patient: No, I have trouble going to sleep and something awakens me; I wake up early, 5 o'clock. My husband is an osteopath, and he doesn't. He works in the evenings, too, so he doesn't start work in the morning till about 11. So he doesn't like to get up early, but I wake up early, and I just have to lie there in bed. Can't go to sleep, toss around. Don't have—I don't have the feeling in my stomach then. Just the last few days it seems to last all night.

Doctor: What do you think about when you are lying there in bed? Any particular thoughts that seem to be on your mind?

Patient: Well—yes, I think mostly about my husband.

Doctor: Your husband?

Patient: Mmm.

Doctor: What about him?

Patient: Well, I suppose I ought to talk about it. It's not going to be easy to talk about. Aaaah—Well, we haven't been getting along very well, oh, for four to five years now. One thing is, he likes to go on vacations that are no vacations for me. He likes to——he likes to go fishing. It used to be fun sometimes when I was younger, but—he—he still likes to go hunting and fishing up in the country, where there are no conveniences; it's all primitive, and it's cold. No fun for me. He goes out and brings enough fish to fill the freezer for a couple of years, and so I just don't get any vacation.

Doctor: Has this always been true during your marriage?

Patient: Mmm. Yes, but I guess I used to be able to go along better than I do now.

Doctor: How long have you been married?

Patient: Well, we've been married—uh—let's see, 26—we've been married—uh (muttering; Makes some calculations here)—26 years.

Doctor: And up until four or five years ago you enjoyed these vacations, did you?

Patient: Mmm. I didn't enjoy them, but I went along. I didn't have the same feeling of tension while I was on the vacation. And he likes to take a couple of people along. Well, I just don't enjoy it, that's all.

Doctor: Friends of his, and friends of yours, too?

Patient: Mmm. They're friends of ours, but we hardly ever see them in between vacations.

Doctor: Is this another couple?

Patient: Another couple, and she doesn't like these vacations any better than I do.

Doctor: How often does he take this type of vacation?

Patient: Every year. Sometimes twice. But I've gotten so I'd just as soon he'd go alone. Of course, he doesn't like that; so then we have an argument about it. Last winter, I just gave up, and I decided I was going to take a vacation like what I like; so I went down to Florida by myself. Sat on the beach.

Doctor: How long were you there?

Patient: Ten days. A wonderful rest. If I had taken my husband, I couldn't do that. He's always got to be doing something. Hunting, fishing—never comfortable.

Doctor: How does he feel about your going down to Florida all by yourself?

Patient: Well, he didn't like it, but he got over it.

Doctor: And you did enjoy that trip?

Patient: Yes, I did.

Doctor: How did you feel when you got back?

Patient: Oh, pretty good for a little while; then the stomach trouble came back.

Doctor: How long had you been back from your vacation when you began to be disturbed by this?

Patient: About a month.

Doctor: About a month. And that was this past spring. Do you have children?

Patient: Yes. Two. I have a boy who is 24, and a girl who is 22. The girl's adopted. She's always been a problem.

Doctor: In what way?

Patient: Well, I don't know. But she was always a problem from the very beginning. She has a temperament that is kind of explosive. Very rebellious and so on. Excuse me (belch). But she's—oh, we have a lot of trouble with her, and she finally decided she was going to leave home and not stay with us any more. She went to the university. Tried to support herself. She's a pretty mixed-up little girl. I've done the best I can for her.

Doctor: When did she leave home?

Patient: About two years ago; no, I guess it was a little longer than that.

Doctor: And she's been attending college and working ever since?

Patient: Uhuh. My son is an aviator. He's married now. Got married when he came out of the service. They can't have any children, for some reason—they had a lot of trouble soon after they got married because of that. She wanted children.

Doctor: How long have they been married?

Patient: Just about two years.

Doctor: And there has been some trouble between them because of this?

Patient: Yes, they have a lot of—unhappiness and so on, and . . . John used to come over and talk to me about it, but there was not much I could do to help it.

Doctor: He used to discuss this problem with you? He was quite concerned about himself? He wanted children?

Patient: Yes, partly because he knew that Mary wanted children, and, he wasn't giving her any children, so, he was concerned about that. They're Catholic. I don't think that they can break up the marriage, although I guess they can.

Doctor: It's been this serious, that there is some danger of the marriage breaking up?

Patient: Hmm.

Doctor: How long has this problem been going on? They've been married two years, and I understand that John has been coming to you and discussing it with you. Has that been for a long time, or just now?

Patient: Well, it started soon after they got married. Partly because, uh——they got married when, just when, he got out of the service, and he was kind of restless then, too. He made a lot of money in the service and he'd gone in just out of high school, and he wasn't prepared for anything when he came out, so that he didn't have any decent job, and he almost went back in the service again; after all, he could make a better living there than he could outside. But he stuck it out, and he's getting along fairly well. It hasn't taken as long as he thought it would. But, uh——she's a kind of selfish girl, and she wanted a lot of things that he couldn't give her in the beginning. That was one thing; and then the children——why?

Doctor: Well, I just wondered how does this affect you? I'm sure that you've been concerned about it also.

Patient: Yes, I've been concerned about it. I feel very unhappy, because John is, uh——pretty important to me. I want him to be happy. I like his wife, but I don't think she's quite up to him; but then I suppose I'm his mother, so I wouldn't.

Doctor: How did you feel about their marriage plans?

Patient: Well, I thought they got married a little bit in a hurry. I thought he ought to take a little time to establish himself before they got married.

Doctor: How did you feel about this girl? Did you approve of her?

Patient: Yes, she's all right.

Doctor: But you didn't feel that she was really . . . .

Patient (interrupting): Oh, I don't think I'm a bad mother-in-law, if that's what you mean.

Doctor: What I wondered is that you mentioned that you didn't think that she was quite up to John, and I wondered . . . .

Patient: Mmm, well I——I,——she's——she's all right.

Doctor: Now you mentioned that you've been having difficulty with your husband for a number of years, but that just last winter you went down to Florida, finally going on a vacation such as you wanted. And then about a month later you developed these abdominal pains and discomfort.

Patient: And they've been pretty continuous ever since then.

Doctor: Was there anything else that happened around that time, last winter and spring, in your life?

Patient: No, I don't think so.

Doctor: There was no change in your activities?

(Silence or muttering)

Doctor: Now, what other difficulties have there been between you and your husband? You speak of this vacation problem.

Patient: Well, of course, we always had some difficulties as far as his family was concerned. He was the only boy, and—and, his sisters, who were older, and his mother all put a lot of claims on him, so that we always had to go over there on Sunday; and I kind of resented that almost from the very beginning, and if there was anything that his mother needed, in the way of money and so on, he'd give it to her even if we had to go without, and so forth, but she died about three years ago. That helped.

Doctor: It does? You don't have to go over there?

Patient: No, we don't have to go over there any more. His sisters, they still seem to make the same kinds of demands on him. They put him on a pedestal and so on, and uh——but he doesn't——go along with them quite so much as he did with his mother. Of course, his father died when he was a child. So he hasn't been around since we got married.

Doctor: What's your husband like? How would you describe him?

Patient: Oh, he's a big fat man . . . not too good-natured, but he usually kind of gives in to people. Not to me, but to other people.

Doctor: Does he let others take advantage of him?

Patient: Yes, I know they do. Patients; his family. The only people that he stands up against is his own family, me, or his son, or his daughter.

Doctor: Is he quite busy in his practice?

Patient: Yes, he's quite busy. He makes a good living.

Doctor: Now your name is Irish. Your husband is Irish?

Patient: Yes, he's Irish.

Doctor: Are you also of Irish descent?

Patient: Yes.

Doctor: Would you tell me something more about your earlier childhood, where your parents are from?

Patient: (Cough; silence)

Doctor: Where were you born?

Patient: Here in Chicago.

Steps in Sequence of Class Discussion with Reference to Teaching Goals

A. At this point, the teacher interrupted the interview to give the class and the therapist a chance to summarize the information received and to begin to interpret it diagnostically.

Teacher: Let's interrupt here for a minute, and gather this together. I think the interview is progressing, but I'd like to stop here before you go into the past history. We will ask the class for their summary of what they know about this woman now, and what they think about her, what are they especially interested in exploring further.

Student A: Well, I would like more information about the vacations, what events actually happened there, what actually occurred on the vacation.

Teacher: Do you think that in this first interview this is something that you would consider pressing?

Student A: I would, in the sense that I think in the very first interview it is very important to give the patient the feeling that you know what you are doing, or that you are getting at something. I think that is very important. It may be more important than getting a complete history in the first interview. I think that if each hour doesn't have some point to it, then it is not so good.

Teacher: You mean if the patient does not have something to take away with her?

Student A: Yes, if somehow you haven't at least had the feeling that you are leading toward something that is important. And the present illness here is the thing that you have to start with.

Teacher: Anybody else have an opinion about that? Would your curiosity point toward the vacations or something else?

Student B: Not that particularly; it doesn't make much difference whether we have more information about this in this interview or in a later one, but more information about what was going on a number of years ago, when most of this all began. It got worse with the vacation, and a number of things all occurred at the same time, or pretty close to the same time, with the daughter going away, and the son going away.

Teacher: You mean you are dating the onset of the present illness back a couple of years, or three years?

Student B: Yes. . . .

Teacher: Although the onset of the more acute symptoms was only last spring?

Student C: I think I would focus even more on the extremely recent present illness because of the way the woman comes in and says: "I'm here because I was sent, and you're a nerve doctor." From this I get the feeling that this woman ought to have quite thoroughly explored every symptom that is going on before you can go back into the past. More time should have been spent on the symptoms of the stomach and the sleeping, and the headaches which were mentioned, and things like that. I had the feeling that the material from the patient came out very easily. I had the feeling that actually the emotional business was gone into much too quickly. From the point of view of therapy it is certainly necessary to get some of this, because you have to know how long you are going to see this woman and what kind of therapy you are going to do with her. You need to get some clues.

Doctor: How do you find out if you don't allow her to express emotions?

Student C: Well, you have to, but you have mixed feelings about this because, on the other hand, you need to get more of the very present material and the symptomatology first; so you are sort of between the devil and the deep blue sea.

B. Observations of Behavioral Dynamics with Opportunity to Discuss Their Meaning

One student began to speculate about the reason why the vacation in Florida seemed to be a precipitant and thought that he would look for some experience on that vacation which might have produced conflict and anxiety. In following up the context in which the subject of vacation had been brought up, however, certain sequences of dynamics became apparent, namely, insomnia, tension about her husband, suppressed anger at him, frustration, resistance, withdrawal, shift to a focus on his lack of consideration for her on vacations—an ego-acceptable subject, defensive in its function. The information here involves several nonverbal cues, the sequence of which is important.

Teacher: Why would you go into the vacations more?

Student A: Well, I think it is a precipitant. I think the other parts of the present illness suggest its importance. The Florida vacation, for instance.

Teacher: Let's take another look at that. You think the Florida vacation was the precipitating factor.

Student A: Well, apparently the symptoms began after that vacation. I don't know if anything else seems to be happening.

Teacher: Well, I would think that you would have something in your mind that you would be looking for in that Florida vacation.

Student A: Yes, I was. I think it is quite likely she was either exposed to some kind of sexual longings or actually had some kind of sexual brush with somebody, I don't know. I would suspect that if nothing else happened around that time, that assuming the daughter didn't leave . . . . I don't know when the daughter left.

Doctor: Two years ago.

Student A: Two years ago. Well, nothing is particularly new with the son; nothing is particularly new with the husband, at least so far as we know now; the big thing seems to be that something happened, and she decided to go to Florida, and following that got symptoms.

Teacher: Could be, but if that's what is in your mind, I think I would go very slowly on eliciting those details; but I do think that the way she introduced the subject of vacations is significant. It was in response to a particular question of yours, if I can remember correctly what happened here. Has anybody else got an observation on that?

Student D: He just asked the general question, what is the trouble, and she said vacations.

Doctor: No, I asked in regard to the husband.

Student D: Well, she became very concerned and somewhat depressed when he asked what she was thinking about in the morning while she was lying in bed, and there was great difficulty talking about it. She shifted on to vacations, which was the general complaint against her husband. I wonder whether it wouldn't be a good idea to explore that more. Of course, she did become quite depressed, and one would have to go quite carefully, but I think that is an area to explore.

Teacher: I am curious about your saying "depressed." Did she become depressed or more withdrawn, in the sense of covering up, with her guard being raised at that point?

Student D: She also seemed to shift from a topic which, while it was a complaint against her husband, was a kind of neutral complaint. It really wasn't; it was bad, but perhaps there are some other complaints that she has that are really bothering her more than the vacations.

Teacher: Or that she has more conflict about. That's an important thing to know the difference between the complaint that she gave you about the husband. He goes off on his vacations; he enjoys himself, but she doesn't. It's cold; it's wet, and they live in a log cabin, or a tent, or something, and she has to cook over an open fire, kind of thing. These are complaints over which she has no conflict, or less conflict than some other complaints about the husband that really bother her more. She has more conflict in telling you, more conflict in even considering it as far as she herself is concerned. I think what happened here involved the dynamics of a little interplay. She says: "I lie in bed in the morning; I wake up early and I have to lie there and toss," and the doctor said: "What do you think about?" and, if I remember correctly, there was quite a pause. She looked at you in a funny way and hesitated and then jumped to the vacation thing. It was almost literally a jump.

Doctor: First she said that she supposes she has to talk about the husband, and then gives this one aspect.

Student A: She was saying, "I really have to start telling you about some of my feelings, not necessarily just the vacation." And that gave me the clue that what she was saying about the vacations was extremely significant, and although she became reluctant and withdrawn, I didn't get the feeling that she was actually distorting.

C. Observation on Nonverbal Behavior in Its Context, with Discussion of Its Meaning; and How the Interpretation of the Meaning Might Influence the Therapist's Technique

Several students had observed the belch; some had not. At first there was confusion as to its place in the verbal context of the interview. There was general agreement that this nonverbal item was on a deeper level in terms of accessibility to awareness of meaning, either to the patient or to the therapist, than some of the other nonverbal cues. Therefore, an active probing at this time was not indicated.

Teacher: Well, this is interesting because I know the answers, and actually the vacations are more of a hat rack than they are the source of the thing. It is true that it is possible that the vacations either in the North Woods or on the Florida beach allowed her fantasies to be stimulated, but actually there is less real trouble there than in another area in her life. This is a good illustration of the fact that something the patient says, especially in the form of a defense and a red herring, has maybe only a little significance in it, or maybe a great deal of significance. You all jumped to the feeling that something happened

on this vacation. What I think is important here is to recognize the play of stimulus and the responding resistance, and the way she handled the demand on her to talk; to observe what she said and how what she said could relieve her tension to some extent. Now the question is: If you evaluate that correctly—namely, that there is tension; she has to relieve it, and this is the way she relieves it—then what happens so far as your thinking goes? What do you have to decide?

Doctor: Whether to continue at the underlying reason for the anxiety or not, or whether to allow the defense to operate at least for the present.

Teacher: Yes, you have to decide that, and this is where we would come perhaps to a difference of opinion. I think in the first interview one might test it further, but perhaps in the first interview one might only recognize that there is something underneath here and question how you are going to help the patient get at it. What kind of procedure, what kind of plan in your work with her, are you going to carry on? Now, what one of you said, is important—that this patient needs a thorough elaboration, if only on a descriptive level, of her symptoms, which means the headaches also. You tried to get at some specific precipitating event for the return of the stomach trouble last spring, without any success. I mean, you got denial. There wasn't anything there, and so on. Is there anything else that anybody wants to comment on this section of the interview?

Student D: I would like to raise for discussion the point about the belch—whether anybody was impressed with that, whether anybody noted what she was talking about at the time of the belch, and if you did notice, or if you were impressed, whether you would have done anything about it?

Teacher: I don't remember when it came up.

Doctor: With the rebellious daughter.

Student B: I had trouble deciding whether this was your belch or the patient's.

Teacher: For the moment, I'm not going to tell!

Doctor: Actually, I thought that if it was the patient, it was certainly significant, and I was impressed by another thing about the daughter. The patient seemed quite concerned about her daughter. And the fact that the daughter was adopted, and the son was having trouble having children, I felt was something to be investigated, but I didn't feel I wanted to push it at this point.

Student E: I think one also got the feeling that she has much more invested in the son than in the daughter. "The daughter is a pretty mixed-up kid," as though she were really somebody far away. The son she was very concerned with. As far as the belch goes, I think that is something to store away in one's memory, but not to interpret at this point. I don't mean interpret, but even to count it.

Student A: Something you could comment on though, was—I would agree that this kind of thing is too unconscious to comment on, but you can talk about things like why it was that she didn't ever want to go on a vacation. Why did she go if she didn't want to? If she is talking about her husband, certain major trends emerge immediately. The things between her and her husband—she describes how she wakes up and he stays asleep; going on vacations she doesn't want to go on; why does she have to, things like that.

D. Observations and Diagnostic Interpretations Unverbalized by the Therapist But Which Influenced His Subsequent Action

This interpretation to himself was an integrating idea and correlated the evidence of the patient's conflict as involving reactions to deprivation, with the possibility that its roots were in childhood experiences. This dynamic line was further developed in subsequent discussion and the next phase of the interview.

Doctor: I thought that an important aspect of the vacation thing was the fact that she, at this point last winter, decided to do something for herself. Something that she wanted to do. This was a shift from the way things had been before. One thing I did consider in that regard was whether she might feel guilty about, not what she did on the vacation, but just the idea that she was doing something that she wanted to do, in opposition to the husband's wishes.

Student A: If she does one thing that she wants to do, then she won't be sure what she will do next—as if she were thinking that—Is that what you mean?

Teacher: But your question (Student A) was to concentrate on why she had not done it before.

Student A: Yes, I think that is the kind of thing one could comment on. One might say: "Why do you say you didn't want to go, and yet you went?" That interpretation would be all right if you wanted to try digging at something, or poking at the relationship in some way. This kind of thing would be much more appropriate to start talking about than signs and symptoms, like the belching and other things which are more deeply embedded.

E. Discussion of the Technique of Intervention and the Relation Between Dynamics and Technique

Teacher: Well, I think you are right, that the belch, to use your words, is deeply embedded. I would like to put that aside for a minute, because the type of question which you are raising is one

which is likely to increase the patient's resistance against you. Why? For one, because she does not know the answers. The reasons for that are probably just as much unconscious as the reason for her belching at this time. There might be other ways for you to expose this facet of her personality, but when you go at it in this way, you tend to put yourself in the position of the inquisitor, not simply the investigator, or, more crucially, the helping doctor.

Student B: . . . you might say something like, "So you've finally decided to do something for yourself."

Teacher: Remarking that, perhaps she wanted to do this before, and that at last she did, or something of that sort. You see, when you make such a frontal attack, on her personality, "Why didn't you do this before?" you are likely to make a patient feel accused, and then she has to resist you, not just her own unconscious. As far as the belching goes, you are quite right; this is a much deeper thing. Deeper in what sense? How would you describe this as a significant clue compared with her remark about the son, for instance, and his wife?—that kind of thing. Obviously, there is some tension involved in both, but what's the big difference, speaking in terms of the dynamics here?

Doctor: The belch is an unconscious symptom which is actually the one involved in her present illness. It would have even more significance because of that.

Teacher: We are assuming that the belch is a symptom. If it is a symptom, then conflicts are involved in it. It is not unconscious. She said, "pardon me." Only the meaning is unconscious.

Doctor: I mean that the reason behind it, the impulse, the conflict, whatever enters into the formation of the symptom, is unconscious. The symptom itself she is aware of, but she is completely unaware of what it represents.

Teacher: And what the belch represents is more unconscious, more deeply buried, with more separation between it and her consciousness, than the remarks about the daughter, and feelings about the daughter especially. So that with anything of that sort, of course, one has to be very careful about making a frontal attack, because you are going to have to batter down whatever defenses are there that separate this from her consciousness of the emotional factors involved . . . as you bring them into consciousness. Anything else?

Student A: One other thing that one might keep in mind was her decision finally to take a vacation by herself after all these years of being unhappy, apparently, with the vacations with her husband. What relationship this has to the growing distance between herself and her son now that he has been married for two years, or whether there is some relationship here?

F. Discussion of the Determinants of the Therapist's Thinking

Questions raised by the teacher to bring out the therapist's tentative formulation of the patient's problem, with the evidence for his opinion and his plan for the next phase of the interview.

Teacher: What you are saying now, of course, is evidence of your evaluation of the facts as she has given them to you, and your observation of her. Which brings me to another point that I wanted to emphasize in the discussion now: You have not gone back into the childhood history yet. I stopped you before you did. One could ask what made you feel that you wanted to go into the past history at that moment. One could also ask, What do you know about this person from the data up to that point? What kind of a person is she? What kind of a problem does she have? How has she dealt with it in her adult life? These are things that not only descriptively but dynamically have to be part of your thinking, and then when you go back and get the evidence from the past, you get evidence that points toward the development of this particular personality, and her ways of solving things that have brought her to this impasse, this pathology at the moment. What can you say about this woman, before we go into her past life?

Doctor: Well, I think that she is a woman who feels deprived. Now, how much actual deprivation there is, I don't know; but she certainly feels that she is not accepted by the husband, not so much not accepted as she feels that he needs her, that he wants her around, but he doesn't give to her, he doesn't meet her needs. She has allied herself with at least her son, she says children, but you do get a feeling that it is the son who is apparently a substitute for some of the things she wanted from the husband which were lacking. I think she is a mother-in-law, in the usual sense. There is a lot of feeling about this other girl; when the wife says that the son doesn't give her a baby, the patient feels the implication that something is wrong with the son. This is a very disturbing thing for this woman. I have a further fantasy, which I certainly would not explore with the patient, but it did occur to me. This was in regard to the symptoms which the woman has, the lump in the abdomen, the belching, and so on, which are symptoms common in pregnancy, and the fact that the son could not have a baby by his wife; perhaps with the mother things would be different.

Then I think that the main thing that impressed me was that this woman felt deprived by her husband and had turned to the son for gratification.

This was interfered with by his marriage, although it was still stimulated because the son kept coming back to her. Then she finally did make a move toward getting something for herself, the vacation, and afterward developed these symptoms. One possibility could be her guilt feeling over whatever getting something for herself means.

The reason I wanted to go back to the past history at this point was to find out if that would be consistent with this idea. Did she feel rejected by her father? Was she a person who had to do things for others in order to feel comfortable, or what? Just what was the background? There are many unanswered questions in the present material, and I think they could be pursued with profit. I don't know, I just felt, I didn't time it, but I wanted to get some further idea in the first interview, so that I can get some confirmation if possible; then I'd know how to pursue the subject further.

Teacher: What can you say about this woman's impulse life?

Doctor: I think she is pretty much repressed, or suppressed, I don't know which. I think that she does not gratify her impulse for one reason or another, in general.

Teacher: What impulse?

Doctor: I think probably the wish to be taken care of is not fulfilled. How much of the taking care of others she does, I don't know, but the impression I have is that she does a good bit of that.

Teacher: What other impulses . . . .

Doctor: (Interrupting) The question I almost asked directly, but decided to wait on, was her sexual life with her husband. I thought that that probably would be pretty unsatisfactory, currently, and probably has been unsatisfactory for some time. I thought she was probably depressd too, and might have some other symptoms of depression.

Teacher: But you are leaving out one big area here. Her hostile and her aggressive impulses. What can you say about those?

Doctor: I think they are bubbling.

Teacher: And what has she done with them, besides belch?

Doctor: She went to Florida; this is one thing I think. . . . Most of the time she pushes them down, but they come out indirectly—a little anger toward the husband which she can't express directly toward him; a feeling that the daughter-in-law is not good enough; a feeling that the husband is not attentive enough on something like the vacations. She doesn't express her anger directly, or even come close to it.

Teacher: Yes, she does express them indirectly. In thinking about this from a more dynamic point of view, you have to consider the problem quantitatively as well as the adaptive angle of it. How strong are these aggressive impulses?

Doctor: They are very strong.

Teacher: You think they are very strong, but yet they are not very freely expressed. She doesn't come out with her fists flying, only her stomach lets go now and then. What else has she done with this quantity of tension, impulse tension?

Student: She lies in bed tossing and turning.

Teacher: She doesn't sleep; that's one thing.

Student: She eats.

Teacher: She eats, but you don't have the evidence that the eating is a way of trying to relieve the tension of the hostility.

Student: She develops somatic symptoms.

Teacher: She develops somatic symptoms. They might not be as much connected with hostility as with conflicts over the longing to be taken care of and the frustration of it.

Doctor: She allows herself to be deprived, and deprives herself.

Teacher: She allows herself to be deprived. Now there is a person that you suspect has been deprived, yet she continues to allow herself to be deprived; this must be her way of solving some other conflict. Conflict over her aggressive impulses, which would then be on another level, wouldn't it? Let's say the need to be taken care of and its frustration might stimulate hostility, aggression, anger, impulses to strike out and get what she wants, and so on and so forth. But this brings her to another area of conflict. She cannot allow herself to express the aggression directly for one reason or another, and so she is dammed up again, and frustrated again, and she solves this by allowing herself to be deprived. The daughter, obviously, is also a source of frustration, for some reason. So you have evidence here of very strong impulses, and lots of her energy has to be spent in controlling them. I suspect, if you were to go into the question of her headaches, you would discover a lot of evidence concerning control of hostility. Let's get back to the patient.

Doctor: Should I continue as I would have at that point, or at least try to as I would have, or should I shift back to the present illness and try to elucidate some of these other questions, such as the headache?

Teacher: No, I think you ought to go on as you would have.

Interview Resumed

Doctor: I wonder if you could tell me something more about your earlier life experiences, your childhood, your parents, and family.

Patient: Well, I was born in Chicago. My father was a carpenter, on the west side. And there were 12 children in our family. I'm the oldest girl.

Doctor: Do you have older brothers? How many.

Patient: Two brothers older than I. I was the third one in the family. And it was a big family, and, of course, my father worked hard, but we didn't have too much. It seems to me there was always another baby around. And, of course, mother, she had a lot of work to do, and I had to help her. Somehow it seems to me, my brothers, the older brothers, she never expected the same things of them that she expected of me. I don't know. What else would you like to know?

Doctor: How much older are they?

Patient: John was about five years older, and I think the next one is about two years older than I am.

Doctor: And then next to you the next youngest is a sister or a brother?

Patient: The next youngest is a sister—I think. My goodness! I never remember!

Doctor: There were so many?

Patient: They just came.

Doctor: About every year or year and a half?

Patient: The youngest child was a sister. Then mother stopped having babies.

Doctor: The next younger sister is about a year or two years younger?

Patient: Yes, about every two years.

Doctor: So that you really had your hands full helping out at home.

Patient: Yes. Of course, I was pretty good in school, and I always wanted to go to college, but that was out of the question.

Doctor: Did your parents go to college?

Patient: No, no, they had to go to work, too. The only one that went to college in our family, and she went to one of the junior colleges in the city, was the youngest one. But by that time everybody else was working and contributing; so she could go. I couldn't even graduate from high school. They told me that wasn't for a girl; so I had two years in high school, and then I went to work for a couple of years, and then I went into nurses' training.

Doctor: What kind of work did you do?

Patient: Oh, I waited on table. Same thing my daughter does now, while she earns her way through college. Of course, we help her some, but she was so mad when she left home that she said she didn't want any money from us; but she takes a little now.

Doctor: When you went to nurses' training, was this something that the family helped you with or not?

Patient: No, they didn't have to help you then. You just went into the hospital, and you lived in the hospital.

Doctor: Did you use the money that you saved for that? Or did you have to give that to the family?

Patient: I gave most of that to the family. I was a good nurse. I got along very well . . . .

Doctor: (Interrupting) How long did you work as a nurse?

Patient: . . . . except for one thing, I had trouble with the supervisor in the OB ward. After I finished, I had planned to stay on for a while; but by that time I was having such trouble with her, and my husband came along, and so we got married.

Doctor: How long had you been working when this happened?

Patient: Oh, I just finished . . . .

Doctor: Just finished.

Patient: You mean when I got married?

Doctor: Yes.

Patient: Just finished.

Doctor: And you quit nursing, you mean, at that point?

Patient: Mmmmm.

Doctor: What about this nursing supervisor? What was the difficulty with that OB supervisor?

Patient: Oh, she was bossy, and I thought I knew some things, and she—well, you know, everybody has to make a mistake now and then, and she thought I was doing something very wrong.

Doctor: Is there a particular incident that caused this?

Patient: No, just a lot of little things piled up.

Doctor: Have you had trouble like that with other people?

Patient: Trouble like what?

Doctor: Like you had with the nursing supervisor.

Patient: Oh, my family thinks I'm bossy.

Doctor: Who in your family thinks you're bossy?

Patient: My husband thinks I'm bossy; my son thinks I'm bossy, and my daughter.

Doctor: How about when you were at home as a child? What did your family think?

Patient: Did they think I was? Oh, I don't think so.

Doctor: You had a good bit of responsibility in the care of the younger children.

Patient: Yes, I had a lot of responsibility.

Doctor: Did they mind you very well?

Patient: Pretty much, yes, except the two older boys . . . . They never did much. But they were kind of lazy.

Doctor: Your father was working hard all through your childhood?

Patient: Yes, but he died when I was 20.

Doctor: When you were 20. How did you feel about that?

Patient: Well, he'd been sick for a while, and he and mother hadn't gotten along for quite a while. He'd been sick with heart trouble for about a year, and I guess I thought it was the best thing that he died.

Doctor: Had your parents been separated?

Patient: Oh, no, they're Catholic. They wouldn't separate. They'd just quarrel.

Doctor: Had this been true all the time, their not getting along well?

Patient: No, they used to get along. When I was little I remember they got along O. K.

Doctor: How about your mother? What was she like? Is your mother still living?

Patient: My mother is still living—80 years old.

Doctor: What was she like when you were a youngster?

Patient: Oh, she was the strongest person in the family, I think. She took on a lot of burdens, and went along. My father was strong, physcially; he could work hard and so forth, but he kind of liked to—it was very important to him to—uh—be friends with people. Occasionally he would play cards or loan money to someone and not get it back.

Doctor: She would take care of most of the decisions in the family, financial affairs and so on?

Patient: Mmm. We always had enough to eat, a place to live, and so on, but I remember one time, in the neighborhood where we were, there was a fire in a house and four children were burned, and I remember thinking at the time, why they couldn't have been our children, because we had so many and nothing really to give them.

Doctor: How old were you at the time?

Patient: About 12. I still think about that sometimes.

Doctor: When is the last time you thought of this?

Patient: Mmmm. I don't know.

Doctor: I mean, in recent weeks? or years ago?

Patient: I don't know. I can't remember. Every now and then I think about it.

Doctor: It must have made quite an impression on you.

Patient: Yes, it did.

Doctor: What did you used to do when you wanted to have a good time as a little girl? Were you able to get out and play very much?

Patient: No.

Doctor: How about the other kids?

Patient: About the most fun I ever had was chasing the ice wagon down the street. Getting chips of ice in the summer time; 'course I always had one kid in one hand and one kid in the other hand.

Doctor: And your older brothers, were they able to go out and play ball?

Patient: No, they couldn't do that either. They had to work, run errands and things. They didn't like to, but they did.

Doctor: Did your father stay home a lot, or did he like to get out with the boys sometimes?

Patient: Oh, he liked to get out with the boys occasionally.

Doctor: Did he drink very much?

Patient: No.

Doctor: But he did used to go out for an evening or so with friends and play cards?

Patient: (Silence) I don't think they ever had a vacation.

Doctor: And neither did you.

Patient: That's right. I never did. Not when I was little. Now I don't like what I get.

Doctor: In your marriage, earlier, you've been married 26 years now—did things go along pretty well or was there some difficutly in the beginning too?

Patient: Well things went along pretty well; he's always made a living.

H. Value of the Participant Observation with the DMI

In the above segment of this interview, the patient's tone of voice, posture, facial expression, and manner of speaking were very significant clues as to the dynamics of her behavior at the moment. There seemed to be more emotion coming through than in some of the previous moments. The class could observe this nonverbal behavior and take it into account in their interpretations to themselves. The active contact with the actual interview which here was available to the class is a most important condition for teaching this mode of communication and its significance.

Doctor: We are going to have to stop for today. Is there anything that you would like to ask me about?

Patient: Well, yes, I'd like to know whether—ah—you think that—ah—my stomach trouble and my headaches, and all of that, is related to anything else. Nerves, the other doctor said.

Doctor: Well, I think this remains to be seen. I can't be certain about it because I don't think we know enough about the problem. But I think that we certainly do know that you have been upset recently, and that you've been unhappy, and there certainly may be some connection. I think we should find out more about this, and it's quite likely that there is a relationship between your feeling upset and having an upset stomach.

Patient: You want me to come back, then?

Doctor: Yes, I would like to see you next week at the same time.

Patient: What do you charge?

Doctor: Well, my usual fee is $15 an hour. Do you feel you could afford that?

Patient: I think so. Next week, then, at the same time. Goodbye, Doctor.

Doctor: Goodbye, Mrs. O'Reilly.

Discussion Resumed

I. Exercise in Evaluating the Dynamics and Genetics in Their Interacting Relationship

Teacher: What did you find out this time?

Doctor: Well, I think that the background certainly is consistent with what seems to be the current problem. That is, that she had a lot of responsibility in taking care of younger children, that she wasn't the only one deprived of a lot of things in the family, but she felt in a rather special way that she got less than the others, with regard to the older brothers, and, interestingly enough, with regard to the youngest. I think that the idea that the youngest sister and her daughter got to go to college when she herself had wanted to so much, when she was capable, in terms of intellectual endowment, is an explanation probably, for a good bit of her feeling toward her own daughter, who is rebellious and does get to go to college. The mother in the family was the strong one, the capable one, and the model for the patient. The father, apparently, was somewhat ineffectual. There was something else that happened when she was 12, but I can't remember, something important.

Teacher: The fire.

Doctor: The fire. Well, this was too perfect, I mean, this is something that we'd come back to maybe a year later, whenever she comes back to it.

Teacher: What do you think about the fact that she told you this in this first interview?

Doctor: It indicates that she is completely unaware of the intensity of her destructive feelings toward people who impose responsibilities upon her, rather than give her what she wants.

Teacher: But the strength of her feeling about it is very great, because it breaks through enough for her to remember this thing recurrently and to remember it when she is talking to you today, and to tell you. But her disassociation is effective enough, so that the full significance of what she's telling you is still disassociated from the feeling, so far as any awareness of it is concerned. So your surmise that she was a deprived person is true, judging from the history. Is there any evidence of what she did about that?

Doctor: Well, she tried to get something of what she wanted as a child, as an adolescent, as a young adult. She did finally go into nurses' training, which is something, apparently, that she wanted. Then she runs into a bossy woman, and I think we have to find out a lot more about this. I'm not satisfied that we really know enough about what happened between her and the nursing supervisor, because it's at that point that this adaptation breaks down and she turns to marriage with her husband, as a way of getting something more.

Teacher: What do you think about going into nursing as a way of handling the kind of deprivation she has had?

Student C: Being a nice litle girl and taking care of the younger siblings; so mother will love her.

Teacher: Taking care of the younger siblings up to that point, and then taking care of everybody else. Actually, she was headed for an OB supervisor's job. There she would be in delive with babies coming all the time. What kind of an integrative mechanism is this?

Student: Reaction formation.

Teacher: Reaction formation, and, how much sublimation is there? Well, this is a question we are not going to have time to answer.

Student B: We don't know, because she wasn't in it long enough to be able to see whether it would be called sublimation.

Teacher: This is just a question to toss out here, because we are not going to have time to discuss components of sublimation and reaction formation in this kind of pattern. But, certainly, there is something there. One would raise the question whether, if she became a nurse and carried it out as a profession, it could continue to serve as a defense, or whether she might break down under the stress and strain of continually having to give to other people, unless she was able to get something for herself. So that at that point she did break away, from giving to other people in the same quantity, anyway, and in the same way, and married her husband.

J. The class ended with a discussion of the depressive components in the patient's personality, and, further, with a report of additional facts regarding her history. In describing the course of the original therapy, the teacher picked up several points which had been raised in class discussion and amplified them in the light of the entire treatment.

Summary

During several years we have studied the goals and methods of teaching psychotherapy and have rigorously attempted to establish the advantages and disadvantages of each existing technique. During the last few years we have devised a new method which

we call the dynamimetic interview. This approximates the raw data of a psychiatric interview in a class situation where observation, interpretation, and technique can be practiced under favorable teaching conditions.

We have presented an extensive example with comments on the teaching goals and learning experiences facilitated by this method. This example is chiefly a demonstration of class participation in the practice of interpretative thinking and therapeutic response. The dynamimetic interview method is suggested as one device among a varied list which the teacher can use to provide particular learning experiences for students of psychotherapy.

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Lysergic Acid Diethylamide (LSD-25) Antagonists

II. Development of Tolerance in Man to LSD-25 by Prior Administration of MLD-41 (1-Methyl-d-Lysergic Acid Diethylamide)

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A. Introduction

It has been shown [1,2] that 2 mg. of crude beef brain extract per milliliter of water blocks the usual effect of 2μg of LSD-25 per milliliter in the outside liquid on the Siamese fighting fish.* The experiments to be reported here are the study of a blocking effect probably produced by another mechanism: the development of tolerance [3] to LSD-25 in man by the prior administration for a period of days of a compound similar to LSD-25. This compound, 1-methyl-*d*-lysergic acid diethylamide (MLD-41), produces in man reactions indistinguishable from LSD-25 but has a higher reaction threshold. It will be shown on the basis of our data that MLD-41 affects both the Siamese fighting fish and man in a manner similar to LSD-25. However, there are important differences; in the fish it is about 1/10 as effective as LSD-25, whereas it is approximately 1/3 as effective in man. Since greater doses of MLD-41 may therefore be given to man without producing toxic or dangerous symptoms, it was thought that the development of tolerance to LSD-25 could be more effectively and safely induced with MLD-41 than with LSD-25. This has been found to be true. These experiments form the basis of this communication. Previous reports giving other data on MLD-41 or related compounds have been made by Cerletti and Konzett,[4] Berde and Cerletti,[5] and Konzett.[6]

B. Method

The bioassay of MLD-41 on the Siamese fighting fish was carried out in the fashion previously described for LSD-25.[2] The percentage response-time curves are the basic data given by the smooth curves in the Figure. The response to MLD-41 was superimposed on the LSD-response curves, as indicated in that Figure. In general, 10 fish were placed in each bottle containing 100 ml. of solution. For further details, the previous paper of this series may be consulted. The number of fish used to determine the response at each concentration of MLD-41 was as follows: 10μg, 29; 5μg, 13; 2μg, 16; 1μg, 39; 0.5μg, 21; 0.2μg, 8; 0.1μg, 39; 0.05μg, 8.

The effect of MLD-41 on man was obtained by giving increasing doses of MLD-41 to a group of test subjects who have been used in the study of LSD-25 for the past three years. The interview and test situation was a protected, social setting at the home of one of us (H. A. A.), similar to that previously used but at home rather than in a hospital laboratory.[7] Both LSD-25 and MLD-41 were administered in purified water U. S. P. or in tap

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Sandoz Pharmaceuticals, Division of Sandoz Chemical Works, Inc., supplied the MLD-41.

From the Biological Laboratory, Cold Spring Harbor, and the Research Division, Central Islip State Hospital.

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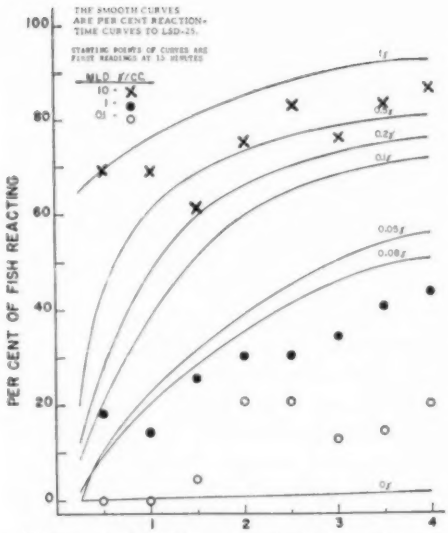
* It has now been found that the fish need not be exposed for a period of hours to the brain extract in order that one may observe the blocking of LSD-25. The brain extract may be added simultaneously with the LSD-25 to the liquid surrounding the fish. The blocking effect is easily observed in this way and strikingly confirms our previous report. It appears on the basis of these data that it is possible that a substance extracted from the brain reacts directly with the LSD-25 in the surrounding liquid. This is also borne out by the fact that the effect of LSD-25 on snails is also blocked by beef brain extract.



Effect of MLD-41 (1-methyl-*d*-lysergic acid diethylamide) on the Siamese fighting fish. Doses are expressed in micrograms (γ).

water, with no essential differences observed between the two.†

The technique of comparing the action of MLD-41 with that of LSD-25 in these subjects was observation and interviewing by means of the questionnaire previously described.[7] The questionnaire consists of a first part, containing 47 questions, and a second part, containing 9 reactions, which are rated both by the subject and by the observer. Positive responses are added irrespective of the intensity of the response. Thus, the numbers in Tables 1 and 2 are positive questionnaire responses and refer to the sum of positive responses to the questionnaire. These numbers, plus the observations of the observer and the trained subjects, constitute the basis for our evaluation of the responses to the drugs.

† The tap water at Cold Spring Harbor does not contain sufficient chlorine to inactivate the pharmacologic activity of LSD-25 materially. As a matter of fact, bioassays with deionized water, purified water U. S. P., and tap water with fairly low concentrations of LSD-25 have shown no differences insofar as their effects on the Siamese fighting fish over prolonged periods are concerned. It should be recognized, however, that if the concentration of chlorine is increased, the LSD-25 will be definitely oxidized. Undoubtedly, purified water U. S. P. is to be preferred. However, we have never noticed any evidences of inactivation in our carefully controlled experiments on fish and on man.

After determining the threshold level to MLD-41 for each member of the group of subjects, MLD-41 was taken at home by our test group five or six days ahead of time in increasing doses. The levels chosen for the first dose were at the threshold of response to MLD-41. Occasionally, slight symptoms occurred at the lower dose, but tolerance to MLD-41 itself developed rapidly. This will be discussed in a subsequent portion of this paper. By giving MLD-41 for several days in advance, protection to LSD-25, induced by administration of MLD-41, could then be studied in blind experiments. However, the dose of LSD-25 finally administered was so high (100μg) that the possibility of suggestion producing the negative reaction observed in this group was eliminated.[8] The doses per kilogram of body weight in these subjects when given 100μg of LSD-25 by mouth were as follows: P. B., 1.33μg; C. G., 1.25μg; M. Z., 1.15μg; D. G., 1.60μg; J. G., 1.65μg.

C. Experimental Results

Effect of MLD-41 on the Siamese Fighting Fish.—MLD-41, as judged by our technique, affects the Siamese fighting fish in essentially the same way that LSD-25 does. The nose up-tail down position is assumed. There are minor modifications in the other reactions, which we do not wish to discuss at this time, since slow-motion pictures are not available. However, the Figure shows that with our earlier criteria for the bioassay of LSD-25, MLD-41 has about $\frac{1}{10}$ the effect of LSD-25 on the fish.

Effect on Man.—Table 1 illustrates the effect of MLD-41 on our five test subjects. In Subject P. B. the threshold was between 50μg and 75μg; in this subject, however, there were 24 positive responses to 35μg of LSD-25 itself. Indeed, his reaction to MLD-41 at 115μg was essentially equivalent to that to 35μg of LSD-25. In subject C. G., who is especially sensitive to LSD-25, the threshold was between 25μg and 50μg of MLD-41. Subject M. Z., however, seemed to be less sensitive to MLD-41 at 75μg, but to have approximately the same sensitivity as Subject P. B. Subject J. G., a woman physician, had a threshold dose of approximately 70μg of MLD-41; with 100μg of MLD-41 the reaction approximated 35μg of LSD-25. The reactions of J. G., there-

TABLE 1.—*Effect of MLD-41 on Man*

Subject and Date	LSD, μg	MLD, μg	Positive Questionnaire Responses			Subject's Dosage Estimate
			First Part	Second Part	Total	
P. B.						
5/25/56	35					
10/12/56		10	24	0	24	Between 25μg & 35μg
10/26/56		25	0	0	0	--
11/9/56		50	0	0	0	--
11/16/56		75	0	0	0	Don't think had reaction
11/30/56		115	12	3	15	Final: Over-all 15μg
			21	1	22	Final: 35μg
C. G.						
5/25/56	35		20	2	22	Final: 35μg
10/26/56		25	0	0	0	Lower than 15μg
11/9/56		50	21	2	23	About 25μg physically
11/16/56		25	0	0	0	Placebo
11/30/56	25		17	0	17	25μg physically
M. Z.						
5/25/56	35		12	3	15	Final: 35μg or better
10/12/56		10	0	0	0	No perceptible reaction
10/26/56		25	0	0	0	No perceptible reaction
11/9/56		50	0	0	0	No perceptible reaction
11/16/56		75	2	0	2	No perceptible reaction
11/30/56		115	30	3	33	35μg
J. G.						
5/25/56	35		5	0	5	25μg or less
10/12/56		10	2	0	2	--
10/26/56		25	0	0	0	--
11/9/56		70	5	0	5	Less than 25μg, threshold
11/16/56		100	7	0	7	--
11/30/56		140	19	2	21	50μg
D. G.						
5/25/56	35		15	0	15	35μg
10/12/56		10	1	0	1	--
10/26/56		25	0	0	0	--
11/9/56		70	0	0	0	No perceptible reaction
11/16/56		100	3	0	3	Like beginning of reaction
11/30/56		140	20	0	20	35μg; maybe more

fore, corresponded to the reactions of P. B. Subject D. G., the least sensitive to LSD-25, was also least sensitive to MLD-41, her threshold probably being somewhat above 100μg of MLD-41.

It is of importance to emphasize that the subjects could not distinguish between MLD-41 and LSD-25 under our conditions.

Blocking Effect of MLD-41 on LSD-25 in Man.—As mentioned in the section on "Methods," MLD-41 was administered in increasing doses five to six days before LSD-25 was administered. A typical experiment may perhaps be one in which, owing to prior administraton of MLD-41, the action of 100μg of LSD-25 was essentially completely blocked (tolerance developed) in our most sensitive subject (C. G.). MLD-41 was administered from Saturday, May 4, to Friday, May 10, starting with 100μg in divided doses on Saturday, May 4, and increasing the dose of MLD-41 by 50μg each day until 350μg of MLD-41 was taken successfully on Thursday, May 9. This indicates, of course, that MLD-41 developed a tolerance to itself. All of the subjects said there were no symptoms whatsoever after taking 350μg of MLD-41 on the last day before the experiment. On Friday, May 10, the day of the experiment, only 100μg of MLD-41 was taken in the morning, with a total of 1450μg of MLD-41 taken from May 4 to May 10, inclusive. On May 10, at 7:45 p. m., 100μg of LSD-25 in purified water U. S. P. was administered orally. There were no positive responses to the questionnaire for a period of three and one-half hours. Subject C. G.'s comment at 8:10 p. m. was: "Estimated dose about 10 μg or 15μg." (This is a subthreshold dose.) "Feeling fine, capable of performing any physical or mental task." At 11:00 p. m. this subject said that he still felt that the dose was subthreshold. All of our data are summarized in Table 2. The data in the Table indicate that MLD-41 taken several days ahead of time by our method protects against fairly large doses of LSD-25, between 1.25μg and 1.65μg per kilogram of body weight.

TABLE 2.—*Comparison of Tolerance Production by MLD-41 and BOL-148*

Subject & Date of Experiment	Total Preparatory Dose of MLD-41, μg	Dates of Administration of MLD-41	Total Preparatory Dose of BOL-148, μg	Dates of Administration of BOL-148	Dose (μg) LSD-25 on Date of Experiment	Positive Questionnaire Responses			Subject's Dosage Estimate and Comment *
						Part I	Part II	Total	
P. B.									
3/16/57	0	--	0	--	50	21	0	21	"Would not like to go alone to Huntington"
3/29/57	0	--	0	--	50	23	6	29	"I have never been so frightened in my life"
4/12/57	900	4/7 through 4/12	0	--	75	0	0	0	"Might have slight LSD reaction; doubt it; would drive car
5/10/57	1300	5/4 through 5/10	0	--	100	1	0	1	Zero LSD
C. G.									
3/16/56	0	--	0	--	50	34	8	42	"Very strong reaction both physical & mental"
5/10/57	1450	5/4 through 5/10	0	--	100	3	0	3	About 10μg or 15μg LSD. "Feeling fine; capable of performing any physical or mental exacting task"
6/21/57	0	--	1000	6/16 through 6/21	50	22	3	25	"Dose estimate 25μg—not mild"
M. Z.									
3/29/57	0	--	0	--	50	33	2	35	25μg LSD
4/12/57	1100	4/7 through 4/12	0	--	80	0	0	0	"No perceptible LSD reaction"
5/10/57	700	5/4 through 5/10	0	--	100	7	0	7	"About 20μg LSD"
6/ 7/5	0	--	1450	6/1 through 6/7	50	14	0	14	"Final estimate of dosage 25μg"
6/21/57	0	--	0	6/16 through 6/21	50	20	1	21	"Estimate 35μg; greater intensity than that of June 7"
J. G.									
3/16/56	0	--	0	--	50	17	1	18	"Onset of effect sharp and definite; greater than 25μg LSD, but not two times"
3/29/57	1000	3/24 through 3/29	0	--	75	0	0	0	
4/12/57	950	4/7 through 4/12	0	--	100	7	0	7	20μg LSD
5/10/57	1450	5/4 through 5/10	0	--	100	3	0	3	"Dreamy—nonspecific"
6/21/57	0	--	950	6/16 through 6/21	50	11	1	12	"Estimate 35μg"
D. G.									
3/11/55	0	--	0	--	25	5	0	5	Slight transient response
3/16/56	0	--	0	--	50	14	0	14	"Unpleasant feelings of rather short duration"
3/29/57	1050	3/24 through 3/29	0	--	75	0	0	0	No reaction
4/12/57	1050	4/7 through 4/12	0	--	100	0	0	0	"No perceptible reaction"
5/10/57	1450	5/4 through 5/10	0	--	100	0	0	0	"No perceptible LSD reaction"
6/ 7/57	0	--	1450	6/1 through 6/7	50	0	0	0	"No perceptible reaction"
6/21/57	0	--	850	6/16 through 6/21	75	12	0	12	"At least 35μg"

* One experiment (BOL-148) of all those performed in this series is not given in this Table. In this experiment, Subject P.B., on the basis of his behavior and his own statements, had a 25μg reaction. However, on his written report he felt his reaction was somewhat less. Since his data would confuse the Table because of the low numerical response on the questionnaire, it is omitted. He stated to one of the other subjects: "I had a severe reaction but did not note it on the questionnaire. I think I had better go back and change my answers."

Comparison of Blocking Effect of MLD-41 and BOL-148 on LSD-25.—In our previous paper it was shown that BOL-148 (2-bromo-*d*-lysergic acid diethylamide) was not as effective as LSD-25 in producing tolerance to LSD-25.[3] Some experiments were conducted with BOL-148 similar to those with MLD-41. These data are found in Table 2. The data show that prior administration of BOL-148 produces some tolerance to LSD-25. In Subject C. G., 1000μg of BOL-148 produced a tolerance to approximately 25μg of LSD-25, so that a 50μg dose of LSD-25 produced a 25μg reaction. This is borne out by data on Subjects M. Z. and J. G., both of whom showed a reaction to 50μg of LSD-25. In preliminary experiments with 1000μg preparatory doses of MLD-41, complete protection was obtained to 50μg of LSD-25. The production of tolerance of LSD-25 by MLD-41 according to data at 100μg LSD-25 doses is about three or four times as effective as that by BOL-148. On the basis of these data, it would seem that the closer the molecule is to LSD-25 itself in its effect on man and on fish, the greater the probability of tolerance production.

D. Comment

The data in Table 2 leads us to believe that if 1000μg of MLD-41 is taken for a period of five days with increasing doses, with a diminished dose on the sixth day, approximately 1000μg of MLD-41 produces a tolerance to about 100μg of LSD-25. In these experiments, and in others previously reported, the dose of LSD-25 per kilogram of body weight is not as important as the personality of the subject in producing the intensity of the response. This is brought out in Table 2, where subject C. G. is our most sensitive on a dose basis but weighs more than any other member of the group. In our previous report on the mechanism of tolerance development by the administration of LSD-25, a mechanism was suggested which assumed that LSD-25 produced tolerance to itself by building up a compound, E_T, which blocked the reaction of LSD-25. The assumption was made that for every molecule of LSD-25 which was administered, a single blocking molecule would develop. Quantitative consideration led to the idea that the way in which tolerance to LSD-25 was lost might lead us to understanding the way in which tolerance in general was developed. Our previous report gives the nature of the mathematical treatment which will now be employed. The effect of a given dose of LSD would be determined by the rate of loss of E_T. If we assume that the reaction velocity of the loss of E_T is of the first order with respect to E_T, we can calculate the loss of E_T and therefore a tolerance to LSD with time, by means of the following equation:

$$\log \frac{A}{A-x} = k_1 t$$

where A is the initial amount of E_T present and x is the amount of E_T lost in time, t. If we assume a velocity constant k_1 representing a loss of 70% of E_T in 24 hours, we may calculate what protection against LSD-25 could be anticipated by taking 1000μg of MLD-41 for five days. This calculation is presented in Table 3. Table 3 has been compiled by following one of our actual experiments, in which 1000μg of MLD-41 was administered with increasing doses so that a total of 1000μg was administered over a period of five days prior to the experiment with LSD-25. It is apparent from Table 3 that, following our earlier assumption, to assume that one molecule of LSD-25 or of MLD-41 produces one molecule of the hypothetical molecule of protective substance E_T representing a loss of 70% of tolerance each 24 hours (ve-

TABLE 3.—*Calculated Tolerance to LSD-25 by Prior Administration of MLD-41, Given by Values of "E_T Remaining"**

Day	1	2	3	4	5	6
Dose of MLD-41, μg	100	150	200	250	300	100
E_T remaining	0	30	54	76	97.8	119

* According to the theory presented, 70% of the tolerance-producing factors, or molecules of E_T, disappear every 24 hours. One hundred nineteen molecules of E_T formed should protect against approximately the same number of molecules of LSD-25. This is in accordance with the observations reported in the text. By extending the experiment for 10 days and increasing the dose by 50μg each day, tolerance to 200μg should develop.

locity constant, k_4) is not inconsistent with the data. Tolerance to LSD-25 is actually built up to approximately 100μg of LSD-25 by the administration of 1000μg of MLD-41. Table 3 serves to show that our theory also accounts for the way in which MLD-41 may produce a tolerance to itself. Thus, on the third day of administration 54 molecules of E_T remaining could easily take care of 200 molecules of MLD-41 because the 200μg was administered over a period of 16 hours.

We believe that the rapid development of tolerance to MLD-41, thus permitting the administration of very large numbers of molecules of MLD-41, might permit development of tolerance to much higher doses of LSD-25 than that observed in our experiments. Experiments of this type are planned. Also planned are experiments with compounds resembling LSD-25, such as the 1-propyl-*d*-lysergic acid diethylamide (1-propyl LSD-25), when and if this is obtainable, since this substance conceivably might be less toxic than MLD-41 but still might provide a means of producing tolerance to LSD-25. Lysergic acid dimethylamide is available and will be studied shortly. These experiments are important for understanding the mechanism of tolerance development and the mode of action of LSD-25. It appears, on the basis of our experiments on fish and on man, that it is primarily the integrity of the diethylamide group that is necessary, but that it is not sufficient for the special features of the LSD-25 reaction. Although BOL-148 has the diethylamide group, the presence of bromine in the 2-position eliminates most of the features of the LSD reaction, decreases its pharmacologic action, and prevents the development of tolerance to LSD, as compared with MLD-41 or LSD-25. On the basis of our data, it would appear that tolerance development might follow administration of molecules spatially related to LSD-25 but also requiring similar pharmacologic activity. It is conceivable that the 1-propyl derivative may have a much higher threshold before producing LSD-25 symptoms and by that virtue produce tolerance more readily.

It is of interest to point out the possibility that the blocking substance E_T hypothesized in this paper might readily be studied experimentally by injecting animals with MLD-41 and searching for LSD-25 inhibitors in the tissues of the animals thus injected. As mentioned in the introduction, such compounds actually exist naturally in beef brain. We are now making a search of various tissues for the presence of similar substances blocking LSD-25, using the Siamese fighting fish technique. Preliminary data indicate that high concentrations of a substance or substances blocking LSD-25 are also found in the spleen and pancreas. This finding will be reported in a separate communication.

The fact that a comparatively nontoxic substance like MLD-41 can produce a tolerance to the more active LSD-25 lends hope to the possibility that if the schizophrenias are produced by a disturbance in biochemical mechanisms analogous to that produced by mescaline and LSD-25, there is good reason to believe that nontoxic molecules might be administered to produce a tolerance to a chemical origin of the schizophrenic state. This may be formalized as follows: (*a*) that there is a substance analogous to LSD-25 involved in schizophrenia, and designated here as P; (*b*) that P has some normal function in the physiology of the emotional processes, but the metabolism of P is disturbed in schizophrenia; (*c*) that the substance P is regulated by a mechanism like the one proposed here for the development and loss of tolerance to LSD-25, and that a breakdown of this mechanism is involved in P getting out of control.

Thus, we would have the mechanism:

$$P+E \overset{k_1}{\rightleftharpoons} \text{Symptoms } PE \qquad (1)\,(5)$$

$$PE \overset{k_2}{\rightarrow} E_T + \text{Decomposition products} \qquad (2)$$

$$E_T + P \overset{k_3}{\rightarrow} PE \qquad (3)$$

$$E_T \overset{k_4}{\rightarrow} \text{Decomposition products or excretion} \qquad (4)$$

where the normal function of P might be involved, for instance, in the accommodation of the organism to stress situations. E_T would be the ballast against emotional explosion, while the reaction k_5 would be the "safety valve" to bring about the necessary emotional response. Without such a safety valve, E_T could act to eliminate P before the organism could make the necessary response.

If we may take the liberty of speculating, a compound methyl-P might produce enough E_T to protect against P and thus modify the clinical schizophrenic state in the same way that 1-methyl-*d*-lysergic acid diethylamide blocks the psychotic state produced by LSD-25.

E. Summary

The effect of 1-methyl-*d*-lysergic acid diethylamide (MLD-41) has been studied in the Siamese fighting fish and in man.

MLD-41 affects both the Siamese fighting fish and man similarly to LSD-25 (*d*-lysergic acid diethylamide). However, there are important differences; in the fish it is about $^1/_{10}$ as effective as LSD-25, and in man the threshold of response is two to three times as high. In the nonpsychotic test group studied, the threshold was approximately 70μg when taken orally.

Tolerance development to LSD-25 was achieved by administering MLD-41 for five to six days before administering LSD-25. The experiments reported indicate that approximately 100μg of MLD-41, administered with increasing doses to 350μg on the last day, protects against 100μg of LSD-25 taken orally.

BOL-148 (2-bromo-*d*-lysergic acid diethylamide) produces tolerance to LSD-25, but the effect for equal weights is much less, approximately one-third that of MLD-41.

The implication of the rapid and effective development of tolerance to LSD-25 by MLD-41 is considered in relationship to a chemical theory of the schizophrenias and the possibility of therapy if the chemical theory is validated.

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Psychopathology and Psychophysiology of Minimal LSD-25 Dosage

A Preliminary Dosage-Response Spectrum

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Despite 14 years of investigation, as intensive as accorded any biologically active chemical, a gap remains in the systematic description of human response to lysergic acid diethylamide (LSD-25). The dramatic schizophrenic-like symptoms after doses of 40μg to 100μg have drawn the main interest. The threshold for activity is placed at 20μg by general consensus, while perfunctory administration of smaller doses has left their effect uncertain.

Accompanying those pharmacologic demonstrations has been the controversy whether LSD symptoms simulate the psychopathology of schizophrenia [1] or can be better explained as a toxic organic psychosis.[2] One of these alternatives might be favored by its resemblance to the complete dosage-response relationship of LSD. It is unfortunate for analogical comparison that early stages of toxic psychosis have rarely been described in a psychopathological framework [3]; on the other hand, there is a firm basis for comparison with various schizophrenic processes.

This preliminary note reports the response to 24 doses of LSD-25, graduated in size to emphasize the relationship of symptoms to dosage.

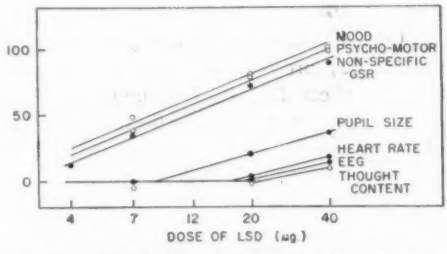
Methods

Fourteen young men without apparent emotional problems volunteered as subjects. Extensive physiological measurements on the subjects reclining alone in a dark room took 20 minutes of each hour. Another third of each hour was absorbed in psychological and psychiatric observation. In the remaining intervals subjects occupied themselves in any way they chose. Conscious mood was assessed by two questionnaires constructed from our initial experiments. On one questionnaire, the subject estimated deviation from his usual state in matters of perception, body image, alertness, emotion, and thought. On the other, the subject placed himself along the scale between pairs of adjectives describing opposite extremes of mood.

A psychiatric interview preceded the dose and was repeated every hour during the experimental day. While the subjects were generally aware of LSD symptoms in usual dosage, none knew the size of their oral dose, or whether they had taken a placebo of plain purified water U. S. P. The "double-blind" system prevailed, in that all measurements and judgments were made without knowledge of the dose.

Results

Physiological changes in general were absent with doses below 20μg. The exception was the nonspecific component of the galvanic skin response (GSR), which was activated after 7μg (Figure).



Effect of LSD dosage on psychiatric and physiological measures. The relative intensity of LSD effects on an arbitrary ordinate are plotted against dose on a logarithmic scale. Measurements are described in the text.

Submitted for publication June 27, 1957.

Department of Psychiatry and Neurology, Baylor University College of Medicine, Texas Medical Center.

This research was supported by the U. S. Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command under Contract No. AF 18(603)-79.

The two questionnaires were marked by four subjects who received 20μg and four other subjects receiving 7μg. After 20μg there were deviations from normal in body image, thought, and emotion at the second and third hours. In contradistinction, after 7μg the subjects did not record departure from their ordinary state during the experimental day.

On the bipolar dimensions of the second questionnaire the four subjects receiving 20μg marked the scales in such a way as to give a decrease in dimensions labeled alertness, motility, control, thought, and sociability. These remained below the initial level for the entire experimental day. On the other hand, after 7μg the bipolar dimensions shifted rapidly. For alertness and motility a dip at the third hour was followed by a climb above the initial value for the rest of the day. Control and thought sank gradually for the first three hours, returning to the initial level at the fourth hour. Sociability increased for the first two hours, dipped sharply at the third hour, and recovered to remain far above the predrug value. The sixth dimension, hedonic tone, also dipped sharply at the third hour and bounced far above the initial level for the rest of the day. These average results from the two questionnaires are described as background for the changes noted during interview.

Psychiatric information elicited each hour was summarized, and symptoms are presented here as representing a "syndrome" if they occurred at a given time in at least half of the subjects who received that dose. Six subjects received the 20μg dose. One hour later they exhibited hypomanic behavior with euphoria, increased psychomotor tension, and distractibility. By the second hour there was indifference with physical retardation and social withdrawal, irritability, and frequent forced laughter without pleasure. At the third hour withdrawal continued with prominent shifts in affect, and changes in thought process, including feelings of inferiority, obsessive thinking, strange unreal thoughts, and one early idea of reference. By the fourth hour most of the subjects were mildly hypomanic and continued that way, with occasional waves of depression or irritability.

In the case of six subjects who received 7μg psychiatric interview in the first and second hours recorded hypomania with expansive euphoria, increased psychomotor activity and tension, and irritability. By the third hour there appeared sudden profound tiredness with an appropriate degree of indifference and depression of mood. At the fourth hour, when subjects were convinced that the drug effects were over, hypomania of a characteristic egosyntonic type developed. Several subjects described this feeling as "rebirth" or "cleansing." Hypomania continued through the rest of the day with occasional waves of depression. There were no changes either of thought processes or of thought content after 7μg (six subjects), after 4μg (two subjects), or after 12μg (two subjects). However, 9 of those 10 subjects displayed cycles of sudden and profound shifts in affect. They ranged toward both extremes of mood during the day; no one experienced severe euphoria who did not also have a high degree of dysphoria at some other time.

The three subjects who received purified-water placebo reported isolated symptoms of tenseness, preoccupation, and change in body image, particularly in the first two hours. The only "50%" symptom for the group was mild sleepiness during the third and fourth hours. In the five subjects receiving doses above 30μg, symptoms were consistent with many reports in the literature, including depersonalization, visual illusions, and suggestions of hallucination.

Comment

The general acceptance of 20μg as the threshold dose of LSD was confirmed for common peripheral autonomic measurements and for dramatic psychic symptoms. However, effects did appear from still lower doses. Though the meaning of the physiological change, nonspecific GSR activation,

is not clear, it has been linked indirectly with neurophysiological arousal by two lines of evidence: the effect of pharmalogic agents [4] and simultaneous estimates of behavioral alertness.[5]

Cycles in affect and in psychomotor activity were elicited by psychiatric interview and by one adjective check list. It is noteworthy that subjects under low doses of LSD were not completely aware of these cycles, for they were not recorded on the other questionnaire, which measured deviations from the usual state. Affect changes have been noted in most human studies of LSD; Stoll's original report [6] includes alternating phases of euphoria and depression from usual doses. The present report distinguishes shifting affect as the mental consequent of low-dose LSD.

Symptoms from LSD in a range of minimal dosage reflect various levels of psychopathology, which cannot be rigorously differentiated from those toxic organic changes occurring before clouding of consciousness. Pending more complete descriptions of early organic symptoms, the spectrum reproduces that of schizophrenia in the following detail. At 7μg rapidly shifting affect simulates the most dependable sign of "trace" schizophrenia, described by Lewis and Piotrowski.[7] In the 20μg range symptoms approximate the pseudoneurotic form of schizophrenia delineated by Hoch.[8] Only above 30μg do classical schizophrenic-like symptoms of visual illusion and hallucinations begin to evolve.

Summary

This preliminary report presents physiological and psychiatric changes in man from doses of lysergic acid diethylamide (LSD-25) below the usual range. Seven micrograms activated the nonspecific galvanic skin response and induced cycles of rapid and profound shifts in affect. Between 7μg and 40μg the dosage response of LSD is consistent with the spectrum of psychopathology associated with the ill-defined group of "borderline" schizophrenic processes.

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Effects of Early Deprivation and Delayed Weaning on Avoidance Learning in the Albino Rat

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Recently the effects of early experience on adult behavior have been the subject of a great deal of experimental work. Several investigators have reported that animals that have received some form of stimulation, noxious, visual, or handling, in infancy appear to be less emotional,[1,2] learn faster,[3,4] and show greater resistance to physiological stress [5] than nonhandled, control animals.

The present study was designed to study, with infrahuman subjects, some of Levy's [6] concepts concerning maternal overprotection. Levy states that "maternal overprotection is synonomous with excessive maternal care of children." One of the criteria for maternal overprotection is "excessive contact, the inseparability of mother and child—manifested in continuous companionship of mother and child, prolonged and excessive nursing."

Few attempts have been made to study systematically the effects of mother-offspring relationships in animals. Seitz [7] reported that offspring from large litters were, in general, more emotional than those from small litters. Levy [8] studied the effects of frustrating the sucking response in infant dogs and found that excessive sucking activities persisted in later life.

The present study dealt with the converse of Levy's experiment, namely, the effects of prolonged sucking and contact with the mother on adult behavior. The behavior under examination was the capacity to learn to avoid an electric shock by traversing through a swinging door to a safe compartment at the sound of a buzzer. The learning of this particular response has been shown to correlate highly with the degree of emotionality prior to learning.[1]

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From the Institute for Psychosomatic and Psychiatric Research and Training of the Micheal Reese Hospital.

Supported in part by the Wiebolt Foundation and in part by research grant PHS M-1051 from the National Institute of Mental Health of the National Institutes of Health, U. S. Public Health Service. Dr. Jacques A. Chevalier gave assistance throughout all phases of this investigation.

Subjects and Procedure

Twenty-eight albino rats were the experimental subjects. They were the offspring of Sprague-Dawley-Holtzman parents. The apparatus was a modified Miller box, described in a previous article.[4]

The animals were placed in four experimental groups. Group LI (N-7) consisted of the rats subjected to late weaning and inadequate diet. These animals were left with the mother until 35 days of life. There was no food available in the home cage. Twice daily the mother was removed and permitted one hour of feeding in a different cage. The group's main source of food was obtained by nursing from the mother. Several times during the prolonged nursing period, supplementary feeding in the form of milk-vitamin-mineral solution was given to these animals. The supplementary feeding was deemed necessary on the basis of the extremely low weights of these animals when compared with normals.

Group LA (N-7) rats were subjected to late weaning and an adequate diet. These animals had the same weaning conditions as Group LI, but had an ad lib. diet made up of the milk-vitamin-mineral solution. For the late weaning groups (LI and LA), two mothers maintained three offspring each, and two mothers maintained four offspring each.

Group NI (N-7) represented a normal-weaning, inadequate-diet condition. These Ss were weaned at the normal time, 21 days of age. From age 21 through age 35 days these Ss were kept on an inadequate diet. The inadequate diet consisted of varying the amount of milk, vitamins, and minerals in solution so that on certain days the Ss might get a full solution and on others they might receive as little

as a 20% to 0% solution. The amount of nutrient solution the animals received was determined on the basis of their weight. The animals were weighed daily, and an attempt was made to keep their weights closely matched to the animals in Group LI. This method of deprivation was used in order to approximate the feeding conditions of Group LI, i. e., a constant but inadequate food supply. One subject died during the deprivation schedule.

Group NA (N-7) represented a normal-weaning, adequate-diet condition. These animals were weaned at 21 days of age and had an ad lib. diet of the milk-vitamin-mineral solution. This diet was used for all animals up to 35 days.

The liquid diet was used for all groups in order to prevent differential feeding experiences, i. e., solid food *vs.* liquid food, during the first 35 days of age. At 35 days of age all subjects were placed on ad lib. Purina Lab Chow until the time of testing, at 120 days of age. Subjects were weighed daily up to 45 days of age.

The adult test procedure was identical with that previously described.[1] The animals were required to learn an avoidance trace conditioning. After being in the apparatus for 1 minute, a three-second buzzer was sounded; 30 seconds after the buzzer was sounded, a shock of 0.6 ma was on continuously until the subject jumped a 1½ in. (3.8 cm.) hurdle through a door. The animal was run until a preestablished criterion of at least eight successive avoidance responses was achieved.

Results

Figure 1 shows the growth curves of the groups through Day 45. By Day 45 all but the LI animals were of equal weight. At 120 days of age all groups were about equal in weight.

Figure 2 presents the number of trials required to reach an established criterion of learning for the various groups.

The differences among the groups were tested by means of the Duncan range test, which arranges means into clusters within which there are no significant differences. The results indicate that Groups LI and LA did not differ significantly from each other, nor did Groups NA and NI. However, Group LI required significantly ($P<0.01$) more trials to reach the criterion than did the normally weaned groups. Group LA also required more trials to reach the cri-

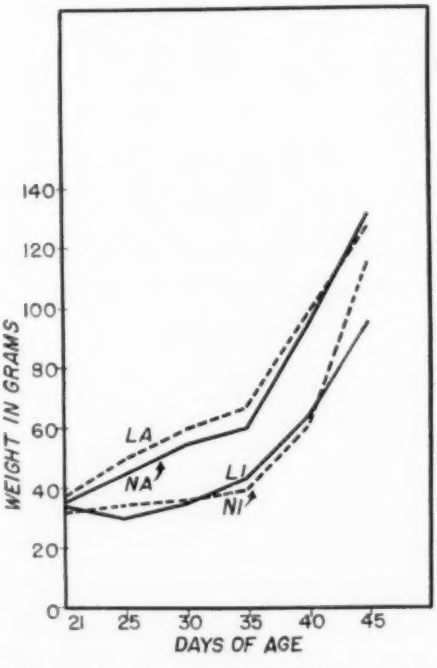

Fig. 1.—Growth curves of the various groups.

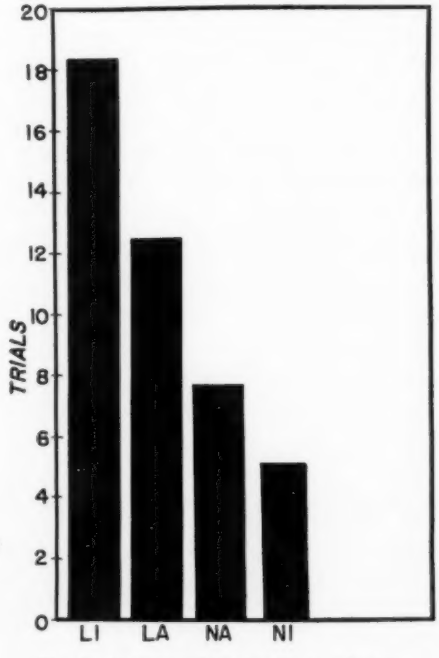

Fig. 2.—Mean number of trials to criterion.

terion than Group NI ($P<0.01$). The difference between LA and NA approached significance ($P<0.10$).

Comment

The results of this experiment indicate the major treatment variable to be prolonged maternal contact. Since neither of the early-deprived groups differed significantly from their respective controls, it is possible to reject early deprivation as a variable affecting the behavior under investigation. However, the animals not weaned until 35 days of age did take significantly longer to learn the avoidance response than the normally weaned groups.

Bovard and Newton[9] reported recently that rats kept with their mothers until 42 days of age defecated more and emitted more vocal responses in a lighted open field than did a normally weaned, control group. Since it has previously been shown that highly emotional animals require longer to learn an avoidance response, the data of the present study and those of Newton seem to indicate the prolonged nursing results in greater emotionality under conditions of stress in adulthood.

These data, therefore, tend to support, in general, Levy's conclusions that one of the consequences of excessive maternal contact is emotional instability.

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Perception of Binaural Beats in Organic and Nonorganic Patients

A. COOPER PRICE, Ph.D.; EPHRAIM S. GARRETT, M.D.; MILES W. HARDY, M.A., and HARRY E. HALL Jr., M.A., Biloxi, Miss.

The diagnosis of cortical brain impairment by means of the visual negative after-image was conducted in earlier experiments, with gratifying results.[3] The Archimedes spiral was used in these investigations to produce the perceptual after-image. The over-all plan was, however, to select or develop a battery of tests which would yield high validity and reliability without requiring too much time to be practicable for inclusion in routine diagnostic examinations. For many reasons the Graham Kendall Memory-for-Designs [2] was selected for investigation and possible inclusion in the diagnostic battery. This test includes a positive after-image, the factor of learning, motor pathways in the drawing of the stimulus forms, a measure of psychomotor coordination, etc. The addition of this test with the Spiral test did raise the diagnostic validity in the determination of cortical brain damage.[1]

Problem

The possibility of the use of other sensory modalities was then considered, resulting in an effort to effect an auditory test somewhat analogous to the visual cortical tests. It was hypothesized that the production of cortical "beat phenomenon" might be perceived by the normals and not reported by the subjects with cortical brain impairment. It was presumed that "cortical beat phenomena" were a result of the higher integrative function of the cortex, and that this function would be impaired in this particular type of brain-damaged patient.

Submitted for publication Sept. 20, 1957.

From Veterans' Administration Center, Biloxi Division.

A research project was conducted by Kent,[4] who used a large sample of patients with known cortical brain impairment. His study has not been published to date, but the results were so generally favorable that this present investigation was designed (1) to test the hypothesis above with regard to perception of the phenomenon by organic and nonorganic patients, (2) to serve as a cross validation for Kent's findings, and (3) to support the inclusion of the auditory test in the projected diagnostic battery if the present results justified.

Method

Subjects.—For the purpose of this study, a cortically impaired subject was defined as one who carried the clinical diagnosis of chronic brain syndrome and obtained "organic" scores on at least one of the two measures of organicity. Fifty domiciliary members of the Veterans' Administration Center at Biloxi, Miss., with known cortical impairment, and satisfying the above criteria, made up the experimental group of this experiment. Their ages ranged from 42 to 72, with a mean of 62 years, 3 months. This group included cases of chronic brain syndromes associated with post-cerebral accident, trauma, drug addiction, chronic alcoholism, cerebral thrombosis, cerebral hemorrhage, cerebral arteriosclerosis, and central nervous system syphilis. The "normal," or control, group was composed of 50 subjects, including employees of the Veterans' Administration Center, members of the domiciliary, and students from evening college credit classes. None of these subjects had a history of cortical impairment, and all obtained "normal" scores on the two measures of organicity.

There were 20 female and 30 male subjects, ranging in age from 20 to 58 years, with a mean of 34 years 8 months.

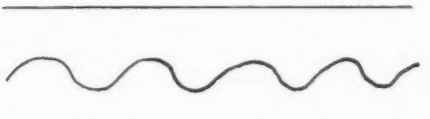
Apparatus.—Two Model 655 Audio Frequency Oscillators, manufactured by the Jackson Electrical Instrument Company, were used to produce the auditory "beat phenomena." These instruments

provide voltages throughout the frequency ranges of 20 to 200,000 cps. Standard conditions of volume at a hearing and comfort range for all subjects were maintained, only controlled fluctuations between 200 and 300 cps being used in this study. Two seats of headphones, one for the subject (S) and one for the experimenter (E), were modified so as to deliver the tone of one instrument (A) to the right ear and the tone of the other instrument (B) to the left ear. The second set of headphones, although not necessary to S's perception of the beat, acted to check the mechanical operation of the instruments, as well as to reassure apprehensive subjects.

Procedure.—Both groups were administered the Memory-for-Designs test and the Spiral Aftereffect test according to Kendall [2] and Price.[3] Each S was then tested for perception of the auditory beat. Ss were set with their backs to the operator and told only that "this was a special kind of hearing test." Headphones, color-coded to identify each ear with its tone source, were placed comfortably over the S's ears. To test the acuity of each subject, they were first asked to "report when you hear a tone and in which ear you hear it." Any Ss failing to demonstrate acuity over the frequency and volume ranges to be used in the experiment were excluded from the sample. A tone of 300 cps was then presented to the right ear and one of 250 cps directed to the left ear. The subject in each case agreed that he was hearing two tones of different frequency or pitch, i. e., one high tone and one low tone. These tones were further described as being "steady" or "smooth." Ss were then told to describe any change they might hear in the "steadiness" or "smoothness" of the tone. To aid subjects in the description of the phenomena, Ss were shown three drawings illustrating three different wave forms and were instructed to use any of the three examples in describing the tone they heard (Figure).

Maintaining a constant tone of 250 cps in the S's left ear, the frequency was slowly and steadily reduced in the right ear through a range of 300 to 200 cps. Most Ss reported immediately a change of volume. This was acknowledged, and they were asked to report any other change in the tone or tones. The frequency at which S reported hearing the phenomena was recorded, as was also the frequency at which S reported the tones to be "straight or level again." A descending and an ascending series of measures were obtained for the right ear by recording the appearance and disappearance of the beat while manipulating the right-ear frequency through 300 to 200 cps and back again to 300 cps.

A similar series of measures were obtained for the left ear by maintaining a 250-cps tone in the right ear and varying the frequency delivered to the left ear. All frequency adjustments were made from the equipment, eliminating any shifting of the earphones themselves. Every effort was made to standardize the procedure for both normal and organic subjects. Except in a few cases, the auditory-beat equipment was operated by the same person.



Drawings to illustrate three wave forms.

Results

Scores of the subjects obtained on the Spiral Aftereffect test are given in Table 1. In general, the results obtained in this study are consistent with the findings of other experiments and by other investigators. Though 90% of the normal subjects earned a score of 4 on this test, only 0.06% of the chronic brain syndrome subjects were able to achieve such a score. While 62% of the chronic brain syndrome subjects failed to earn a score of greater than ½, all of the normal subjects were able to do so.

A comparison of the ability of organic and nonorganic subjects to experience the binaural beat is offered in Table 2. Only 24% of the organic group reported experiencing the beat, as compared with 98% of the normal group. The *t*-test of differences between percentages experiencing the phenomena for the two groups is significant beyond the 0.01 level of confidence.

Evaluation of the effectiveness of the three measures of organicity (as agreeing with psychiatric diagnosis) singly and in combination, as well as the contribution of

TABLE 1.—*Spiral Test Scores*

Score	CBS * Subjects †	Normal Subjects †
0–½	31	0
1–1½	8	0
2–2½	4	2
3–3½	4	3
4	3	45

* Chronic brain syndrome patients.
† N–50.

TABLE 2.—*Comparison of Performances of Organic and Nonorganic Subjects on the Binaural Beats Test*

CBS Subjects *			Normal Subjects *					
No. Experiencing	% Experiencing	σP	N Experiencing	% Experiencing	σP	σDP	DP	t
12	24	6.46	49	98	1.98	6.32	74	11.63 †

* N–50.
† Significant beyond the 0.01 level of confidence.

TABLE 3.—*Comparison of Effectiveness of Three Measures of Organicity*

	Kendall *	Spiral *	Auditory *	Kendall Spiral *	Kendall Spiral Auditory *
N *	44	42	38	47	48
% †	88	84	76	94	96

* N–50.
† Figures reported represent extent of agreement between various measures and clinical diagnosis.

perception of binaural beats on a multiple prediction basis, is presented in Table 3.

The Graham Kendall Memory-for-Designs test accurately diagnosed 88% of the cases; the Spiral Aftereffect test, 84%, and the Binaural Beats test, 76%. The Graham Kendall and the Spiral tests together revealed 94% of the cases, and the three measures together, in combination, 96% of the cases. Many cases are not common to the percentage reported for the various measures, so that in the event one test of the battery failed to agree with the established diagnosis, one or more of the other tests indicated the impairment, thus resulting in increased effectiveness in determining cortical impairment.

Comment and Conclusion

The three tests used in this study have a common factor which accounts for considerable overlay. In addition, each test makes a unique contribution to the accuracy of diagnosis.

The report of perception of binaural beat phenomenon is a valid test for diagnosis of cortical brain impairment.

It is assumed that the perception and reporting of this auditory phenomenon are dependent upon the integrative function of the cerebral cortex. Organic impairment is believed to bring about a reduction of this integrative function, similar to that occurring in the perception of apparent motion and related phenomena.

By testing a multiplicity of functions of the cerebral cortex, these three tests together increase the validity and reliability of the diagnosis of cortical brain impairment.

Veterans' Administration Center.

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Criteria Distinguishing Parents of Schizophrenic and Normal Children

An Initial Study with the Interpersonal Diagnostic System

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Introduction

The study reported here is one of several attempting to differentiate between families having a mentally ill member and those that do not.

In this study my colleagues and I have evaluated some perceptions, attitudes, and values of experimental and control subjects without reference to genetic and circumstantial contributes. The largely experimental data derived by the Interpersonal Diagnostic System of Leary,[1] describing personalities of parents of schizophrenic children, were compared with data describing parents of adequately functioning children of approximately the same age and religious and socioeconomic background.

Material

1. *Patient-Parent Group.*—This consisted of five marital couples, having at least one schizophrenic child, the children ranging in age from 5 to 9 years. Careful physical, neurological, and laboratory examinations did not reveal evidences of specific organic disease. Psychological testing of these parents provided diagnoses ranging from mild personality trait disturbances to neurosis or latent schizophrenia. The parents had some type of individual or group psychotherapy at the Institute and were initially motivated to cooperate in the research studies. In several instances, mild overt resentment was encountered, but all parents completed the battery of tests.

2. *Control Parents.*—This group consisted of six marital couples who volunteered to act as controls. They were recruited from the membership of a Parent-Teacher Association group in a local public school. The following were the criteria for selection of these subjects:

(*a*) They had two or more children, one of whom was enrolled in the public school and was approximately of the same age as the child in the patient group.

(*b*) Their children were at a grade level compatible with their own chronological age, with fairly good relationships to peers and teachers.

(*c*) The children exhibited no obvious behavioral problems or neurotic symptoms recognizable by school personnel (principal, teachers, and nurse).

All parents in this group appeared highly motivated to participate; and when the initial attempt to complete all tests for all subjects at one sitting failed, there was no problem in arranging for extra sessions.

Method

The system of personality evaluation which was used is described by Leary.[1] The theoretical basis of this system is derived mainly from Sullivanian concepts of interpersonal relations. To measure behavior in terms of adaptation, a multidimensional system of personality was devised by which categories of reaction were operationally defined, reliably derived, and integrated at the several levels of personality observed. By this method, five specific levels of personality functionings were systematized and correlated. Table 1 indicates the definition of these levels and the material from which they were derived.

Data for all levels of personality tested are schematized on a circular graph representing a spectrum of behavioral and attitudinal traits. This graph is based on the concept that behavior can

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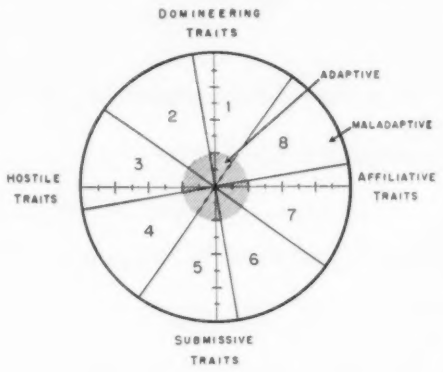
In this study, Donald Klein, M.D., Associate Research Scientist (Psychiatry) offered many helpful criticisms and ideas; Miriam Perr, B.S., and Eleanor Alesi, R.N., B.S., administered tests and correlated data; Sam Campbell, Ph.D., gave statistical aid; W. Offenkrantz, M.D., his encouragement and guidance, and J. R. Whittier, Director of the Institute, suggestions and assistance.

TABLE 1.—*Five Levels of Personality Functioning and Materials of Derivation*

Levels	Definition	Sources
I	Public communication—the interpersonal impact of the subject on others	1 MMPI indices * 2 Interpersonal check list 3 Interview materials
II	Conscious description of self and others—the subject's viewpoint	1 Interpersonal check list * 2 Interview and biographical material
III	Preconscious symbolization—the subject's autistic, projective, fantasy, and symbolic productions. (Two sublevels describe "hero" and "others")	1 TAT story ratings * 2 Dreams 3 Fantasies 4 Other projective tests
IV	Unexpressed unconscious—not yet standardized	
V	Ego ideal—subject's standards and values	1 Interpersonal check list *

* Asterisks indicate material used in this study.



OCTANT	ADAPTIVE DESCRIPTION	MALADAPTIVE DESCRIPTION
1	Managerial	Autocratic
2	Competitive	Exploitive
3	Blunt	Aggressive
4	Sceptical	Distrustful
5	Modest	Self-effacing
6	Docile	Dependent
7	Cooperative	Overconventional
8	Responsible	Overgenerous

Fig. 1.—Graphic schema for the Interpersonal Diagnostic System.

be described in terms of degrees of dominance-submission and hostility-lovingness. Leary states: "When dominance-submission was taken as the vertical axis and hostility-affection as the horizontal all of the other generic interpersonal factors could be expressed as combinations of these four nodal points. The various types of nurturant behaviour appeared to be blends of strong and affectionate orientations to others. Distrustful behaviours seemed to blend hostility and weakness."[2] "Extensive validation of the circular continuum has demonstrated that it is satisfactorily congruent with empirical facts."[3] Originally, a list of traits was arbitrarily collected and was gradually modified to the present 128-item interpersonal check list, which describes eight categories of behavior in terms of adaptive and maladaptive degree. These categories are shown in Figure 1.

All data that were derived from the interpersonal check list, the indices of the Minnesota Multiphasic Personality Inventory (MMPI), and the Thematic Apperception Test (TAT) were analyzed in terms of these eight categories, then quantified and schematized on the circular graph. The raw data in this study were as follows:

1. *MMPI.*—The full 550 cards were sorted individually and scored. The indices for domination (DOM) and lovingness (LOV) were derived from the following fomulas, using *t*-score values for each scale:

$$\text{DOM (vertical index)} = (M_a - D) + (Hs - Pt)$$

$$\text{LOV (horizontal index)} = (K - F) + (Hy - Sc)$$

2. *Interpersonal Check List.*—This is a true-false list of 128 phrases which are answered by the subject about five separate perceptions: of self, mother, father, spouse, and ego ideal. The grouping of these 128 statements into the aforementioned 8 categories of 16 items each allows for quantification of each subject's characteristics. After application of the following formulas, the results are plotted on the circular graph (the numbers refer to octant designations, indicated in Figure 1).

$$\text{DOM} = 0.7(2+8-4-6)+1-5$$

$$\text{LOV} = 0.7(6+8-2-4)+7-3$$

3. *Thematic Apperception Test.*—Ten cards * were shown the subjects, who then wrote a brief story of the action suggested, the people involved, and the anticipated outcome. Each story was then coded on the basis of interpersonal mechanisms by two raters. Where disagreement occurred, discussion resolved the differences of opinion. Usual traits and reactions for both "hero" and "others" were obtained, which were then handled in the same manner as the check-list data, indices for DOM and LOV being derived by the formulas described above for the MMPI.

For each subject, data from these three sources, check list, TAT, and MMPI, were converted into eight variables, which were identified by their location on the octant graph. Thus, a subject might describe himself as modest, his mother as self-effacing, his spouse as domineering, his father as domineering, etc. Each such percept was called a variable, and the relationship between any two is a variability index. In the above situation, the subject identifies spouse and father, strongly disidentifies mother and father, and closely relates

* For men: Cards 1, 2, 3bm, 4, 6bm, 6gf, 7bm, 12m, 13mf, and 18bm. For women: Cards 1, 2, 3gf, 4, 6bm, 6gf, 7gf, 12m, 13mf, and 18gf.

TABLE 2.—*Operational Definition of Thirty-Two Indices of Variation* *

	This Variability Index Is Operationally Defined by Discrepancy Between:			Low Discrepancy Between the Two Measures is Called:	High Discrepancy Between the Two Measures Is Called:
	Level	*Vs.*	Level		
1	I Self	—	II Self	Self-perception	Self-deception
2	II Self	—	II Mother	Conscious identification (maternal)	Consc. Disidentif. (mat.)
3	II Self	—	II Father	Conscious identification (paternal)	Consc. Disidentif. (pat.)
4	II Self	—	II Spouse	Conscious identification (spouse)	Consc. Disidentif. (spouse)
5	II Mother	—	II Father	Maternal-paternal equation	Mat.-pat. disequation
6	II Mother	—	II Spouse	Maternal-spouse equation	Mat.-spouse disequation
7	II Father	—	II Spouse	Paternal-spouse equation	Paternal-spouse disequation
8	II Self	—	III Hero	Preconscious duplication	Preconscious repression
9	II Mother	—	III Hero	Cross-level identification (mat.)	Cross-level disident. (mat.)
10	II Father	—	III Hero	Cross-level identification (pat.)	Cross-level disident. (pat.)
11	II Spouse	—	III Hero	Cross-level identification (spouse)	Cross-level disident. (spouse)
12	II Self	—	III Other	Cross-level identification (other)	Cross-level disident. (other)
13	II Mother	—	III Other	Cross-level identification (mat.)	Cross-level disident. (mat.)
14	II Father	—	III Other	Cross-level identification (pat.)	Cross-level disident. (pat.)
15	II Spouse	—	III Other	Cross-level identification (spouse)	Cross-level disident. (spouse)
16	III Hero	—	III Other	Preconscious identification	Preconscious disidentification
17	II Self	—	V Ideal	Self-acceptance	Self-rejection
18	II Mother	—	V Ideal	Maternal idealization	Maternal devaluation
19	II Father	—	V Ideal	Paternal idealization	Paternal devaluation
20	II Spouse	—	V Ideal	Spouse idealization	Spouse devaluation
21	III Hero	—	V Ideal	Preconscious hero idealization	Preconscious Hero devaluation
22	III Other	—	V Ideal	Preconscious "other" idealization	Preconscious other devaluation
23	I Self	—	I Other	Role coincidence	Role reciprocity
24	I Self †	—	II Mother	Social identification (mat.)	Social disident. (mat.)
25	I Self †	—	II Father	Social identification (pat.)	Social disident. (pat.)
26	I Self †	—	II Spouse	Social identification (spouse)	Social disident. (spouse)
27	I Self †	—	V Ideal	Social idealization	Social devaluation
28	II Spouse †	—	II Parent opposite sex	Spouse-opposite sex parental equation	Spouse-opposite sex parental disequat.
29	I Self †	—	II Parent same sex	Social identification (same sex parent)	Social disident. (same sex parent)
30	I Self †	—	Parent opposite sex	Social identification (opp. sex parent)	Social disident. (opp. sex parent)
31	II Self †	—	Parent same sex	Conscious identification (same sex parent)	Conscious disident. (same sex parent)
32	II Self †	—	Parent opposite sex	Conscious identification (opp. sex parent)	Conscious disident. (opp. sex parent)

* Modified from Leary, T.: Interpersonal Diagnosis of Personality, Table 2, page 254, by permission of the publishers, The Ronald Press Company.
† Added variable indices with suggested definitions.

self and mother. The variability indices in this study totaled 32 for each subject and are listed and defined in Table 2.

For instance, in this system the discrepancy between self-description and preconscious hero (IIS—IIIH) is defined as repression. The relationship of self-description and one's impact upon others (IM—IIS) is an indication of self-perception. Where the variables are alike, located in the same or adjacent octants, the subject perceives himself as others see him; where they differ, there is misperception of self, or self-deception.

In his publication, Leary uses the term "identification" to mean a spatial relationship of two variables no greater than adjacent octants. Thus a variable in Octant *2* would be defined as identified with variables in Octants *1, 2,* and *3* and disidentified with variables in Octants *4, 5, 6, 7* and *8*. By implication, variables in Octants *1* and *3* are more closely identified than variables in Octants *1* and *5*.

When the variability indices for each subject were obtained, comparison between the two groups was possible by several methods.

1. For each variability index, the number of subjects identifying the variables in the experimental and in the control group was obtained. Thus, 4 of 10 patient-parents might identify perceptions of mother and father, as compared with 5 of 12 in the control group. By the χ^2 method to test the significance of differences, the probability of chance agreement or disagreement could be stated. In this instance, there would be no significant difference between the two groups.

2. To establish the specific relationship between variables located in different octants, Harvey and Leary used a scale ranging from 0 to 114.[4] When two variables are in the same octant, the discrepancy value is zero; when they are most distant from each other, e. g., Octants *1* and *5*, the index would be 114. For a single variability index we can obtain an average discrepancy value for all the subjects in the experimental group and compare it with the average discrepancy value of all the subjects in the control group.

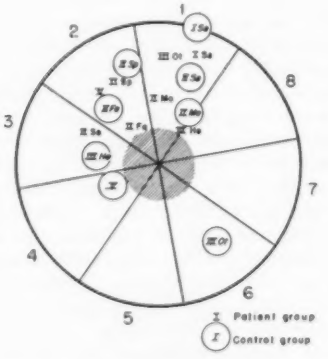
The definition of "identification" in this study relating to diagnoses in adjacent octants coincides with a numerical value of less than 48 on the scale. Values of 48 and greater indicate "disidentification." If, for example, all members of a group had an average discrepancy value of 44, as compared with 50 for another group χ^2 would indicate a statistically significant difference between the two, as one group by definition would be largely identified and the other largely disidentified. However, the actual numerical difference would be small. Similarly, a large numerical difference between two groups, when both fell on the same side of the dividing point, would appear to be indicative of difference between the two groups,

while χ^2 would not corroborate this significance statistically. The discrepancy values for the subjects in each group were ranked according to the method of unpaired replicates and the probability values obtained.[6]

Results

1. The average diagnoses for the patient-parents and the controls are listed in Figure 2. Patient-parents' self-descriptions indicated hostility and less strength than did those of the control parents[1] (Octant *3* compared with Octant *1*).

The symbolic hero (*IIIH*) of the patient-parents was strong and controlling as compared with the more hostile and aggressive hero of the controls (Octant *8* as against Octant *3*), and the patient-parents' symbolic "others" (*ot*) were domineering and strong as compared with the loving, giving traits in the control "others" (Octant *1* to Octant *6*). The patient-parents tend to cluster their perceptions in three octant diagnoses, whereas the controls exhibited more dispersion, using five octant diagnoses.



OCTANT DIAGNOSIS FOR EACH GROUP

VARIABLE	AVERAGE OCTANT GROUP	
	PATIENT GROUP	CONTROL GROUP
I Self	Managerial-Autocratic	Managerial-Autocratic
II Self	Blunt-Aggressive	Managerial-Autocratic
III Hero	Responsible-Overgenerous	Blunt-Aggressive
IV Other	Managerial-Autocratic	Docile-Dependent
V Mother	Managerial-Autocratic	Managerial-Autocratic
VI Father	Competitive-Exploitive	Competitive-Exploitive
VII Spouse	Competitive-Exploitive	Competitive-Exploitive
VIII Ideal	Competitive-Exploitive	Blunt-Aggressive

Fig. 2.—Diagnoses of the patient-parents and control groups.

TABLE 3.—*Comparison of Patient and Control Groups (χ^2 Method)*

Variability Index	No. of Ss Identifying the Two Variables			
	Patient-Parents N=10	Controls N=12	χ^2	*P*
1 IM-IIS	4	10	2.87	0.05-0.10
2 IIM-IISp	7	4	2.95	0.05-0.10
3 IIM-IIIO	5	1	3.09	0.05-0.10
4 IIH-IIIO	6	1	4.48	0.02-0.05
5 IM-V	6	2	2.55	0.10-0.20

2. Thirty-two variability indices were compared by the unpaired replicate method[5] for each group, control parents generally showing greater discrepancies than the patient-parents. With an *N* of 32 in this study, the likelihood of this result being due to chance is less than 1 in 100 (data will be provided upon request).

3. Since 32 variability indices were studied, 6.4 would have been expected to show difference at or below the 0.2 level of significance by chance alone. Five were actually found to discriminate between the two groups at or below this level. However, the specific nature of these indices suggests that they may be of heuristic value (Tables 3 and 4).

4. The variability index of self-perception is defined as the relationship of a subject's impact on others, the social or public level of communication (IM), and the subject's private appraisal of self (IIS). Ten of twelve control parents identified these two perceptions, as compared with four of the patient-parents ($P=0.05-0.10$). Because of two groups clustered closely about the arbitrary point separating "identification" from "nonidentification," the numeri-

TABLE 4.—*Comparison of the Average Variability Discrepancies*

Variability Index	Patient-Parents N=10	Control Parents N=12	*P* *
1 IIM-IISp	38.3	76.2	0.05-0.10
2 IIM-IIIO	48.3	85.5	0.01-0.02
3 IIH-IIIO	39.8	73.6	0.05-0.10
4 IIF-IIIO	51.4	81.3	0.05-0.10
5 IISp-IIIO	50.2	76.5	0.05-0.10
6 IM-V	56.3	75.5	0.02-0.05

* Based on 10 random controls; to equalize the number in both groups by method of unpaired replicates.

cal difference between the two groups was small. Randomly discarding one control couple, $P=0.05-0.10$ is obtained by the unpaired replicate method.[5]

5. The preconscious idealization index defines the relationship between symbolic "hero" and symbolic "others." Patient-parents identified the two in 6 out of 10 instances, while the control parents did this in 1 of 12, ($P=0.02-0.05$). Here, when the average discrepancy values for the two groups were compared, a large difference was noted—73.6 for controls, as compared with 39.8 for the patient-parents ($P=0.05$, unpaired replicate method[5]).

6. The term cross-level identifications refers to a group of variability indices comparing two levels of perceptions about others. Conscious assessment of mother, father, and spouse are compared with the preconscious evaluation of "others." Control group parents identified their mother with preconscious "others" in 1 of 12 instances, while patient-parents did so in 5 of 10 ($P=0.05-0.10$). This result compared with the great difference in the average discrepancy values, 85.5 for the controls, as compared with 48.3 for the patient-parents ($P=0.01-0.02$). Patient-parents perceived their fathers as more closely identified with preconscious "others" than the control parents did ($P=0.05-0.10$).

7. The group of indices of conscious identifications relates the subject's perceptions of specific subjects to each other, such as mother-father, mother-spouse, father-spouse, etc. In 7 of 10 instances, patient-parents perceived their mothers and spouses as being alike, while the control parents did so in 4 of 12 ($P=0.05-0.10$). When the average numerical values for the two groups were compared, the patient-parents were 38.3 as compared with 76.2 for the controls, corroborating this difference between the two ($P=0.05-0.10$).

8. The ego-ideal group of variables consists of comparisons of each subject's conscious ideal with other perceptions. The only significant index was that of the subject's social impact (IM) with the ideal (V). The patient-parents made this identification in 6 of 10 instances, while the control parents did this in 2 of 12 ($P=0.10-0.20$). The numerical average was 56.3 for the patient-parents and 75.5 for the controls ($P=0.02$ by the unpaired replicate method[5]).

Comment

Attempts to distinguish between parents of schizophrenic patients and the parents of normal or adjusting subjects have been reported. Many studies purport to show such a difference, but few have been on the basis of controlled comparisons. In 1949 it was reported by Tietze[6] that 25 mothers of adult schizophrenics, whose cooperation could be enlisted, were found to be either hostile or controlling in their relationship to the therapist; or extremely docile, submissive, and anxious. Acknowledged marital unhappiness was admitted by 12 mothers, but 9 others who declared their marriages to be perfect gave evidences of underlying conflicts. This was a study about which the author said: "In order to arrive at valid conclusions it would be necessary to compare the twenty-five mothers of this series with a control group consisting of mothers who have never produced a schizophrenic child." She felt that difficulties in obtaining this type of control material made such a comparison almost impossible to achieve.

Lidz and Lidz[7] studied the family environment of 50 schizophrenic patients at the Henry Phipps Psychiatric Clinic. Such factors as marked domestic strife, psychotic and mentally ill parents, and frequent instances of bizarre child-rearing habits were found. In fact, only 5 of the 50 patients were felt to have had a reasonably stable environment. Piling up of adverse intrafamilial forces were the major factors in molding a misshapen personality. It was assumed that abnormality of the early environment had a direct bearing on the seriousness of the emotional illness and that the degree of personality disorder prevented

the patient from fitting into the patterns habitually offered by society. This study did not have any comparable control data, but pointed to the possible pernicious impacts of experiential and circumstantial factors.

In 1950, Gerard and Siegal [8] reported a control study in which parents of adult male hospitalized schizophrenics were compared with the parents of functioning high school male subjects of approximately the same age. Although there were methodological difficulties, significant differences between the two parental groups were found. These had to do with the personality traits of the parents, the quality of the mother-patient relationship, paternal relationship to family, and the presence or absence of such traits as overprotection, parental indulgence, prohibition of socialization of the child with others, and anxious and nervous traits.

Mark,[9] in 1953, compared the attitudes on child rearing and child behavior of mothers of male schizophrenics and of mothers of nonpatients where such variables as age, religion, education, and socioeconomic status of the subject population were controlled. Mothers of schizophrenic patients were restrictive in their way of controlling their children's limited freedom of choice, needed to know what the child was thinking, and showed ambivalence between excessive devotion and cool detachment. Of 136 items in this child-rearing attitude survey, 67 were significant at the 5% level of confidence.

We attempted to distinguish the parents of atypical children from the parents of adequately functioning children on the basis of interrelationships with, and attitudes about, self and others. We used the method of evaluation described by Leary. We excluded knowledge about biographical, genetic, and circumstantial data. Intrapsychic conflict and content was our focus. Our results, while not statistically conclusive, appear to corroborate current theories of personality and character development.

In the matter of self-perception, the patient-parents tended to misperceive their impact on others. Might it not be that these sick children, in responding to parental façades, caused anxiety and tension in their parents, who were anticipating different responses based on their own self-awareness? In this instance a situation like that described by Bateson et al.[10] might prevail. This situation, "the double bind," is a transaction between two or more persons involved in an intense emotional relationship, where two orders of conflicting messages are being simultaneously emitted, which demand responses incompatible with each other. Bateson states (page 256):

> We hypothesize that the family situation of the schizophrenic has the following general characteristics:
>
> 1. A child whose mother becomes anxious and withdraws if the child responds to her as a loving mother. That is, the child's very existence has a special meaning to the mother which arouses her anxiety and hostility when she is in danger of intimate contact with the child.
>
> 2. A mother to whom feelings of anxiety and hostility toward the child are not acceptable, and whose way of denying them is to express overt loving behavior to persuade the child to respond to her as a loving mother and to withdraw from him if he does not. "Loving behavior" does not necessarily imply "affection," it can, for example, be set in a framework of doing the proper thing, instilling "goodness" and the like.
>
> 3. The absence of anyone in the family, such as a strong and insightful father, who can intervene in the relationship between the mother and child and support the child in the face of the contradictions involved.

This intrapsychic conflict in the patient-parents studied was evident also on a deeper level of personality organization. The symbolic, or private, "hero" and "others" were closely identified when compared with the control group. Assuming that these identifications refer to early perceptions of self and others, it suggests that patient-parents did not differentiate themselves from others in their own process of maturation. Rank [11] states:

> For the process of individuation or ego identity to take place, it is necessary for the child from the earliest months of life to have a parent or

parent figure who is sensitive to his needs and able to give him at least a minimal amount of consistent affection and support, thus contributing to his feeling of confidence in himself and in the world around him.

The parents in our study, themselves unable to evolve realistic perceptions, were only able to provide conflicting identifications for their children.

The patient-parents saw symbolic "others" as predominantly domineering and hostile, identifications which might create the perception pattern of a hostile, fearful world for their children. This feared world might then drive parent and child into a self-protective symbiosis. This perception of a hostile world might also be a naïve and rigid projection of their own experiences.

Horney [12] stresses the concept of basic anxiety in which a prevailing attitude of fearful and insecure expectancy arises and is perpetuated when an infant or child feels helpless and alone in a potentially hostile world. Arieti sees this as a failure of the child to develop a basic trust in those about him. He says [13]:

In the childhood of schizophrenics this basic trust is lacking or defective, either because the parents are rejecting or because they themselves are extremely anxious, that is, deprived of sufficient basic trust, which consequently cannot be transmitted to the child. The child, on the contrary, incorporates a tremendous amount of anxiety.

Interestingly, such parents identified their spouses with their mothers, thus apparently continuing a conflict-ridden mother-child relationship into the marital sphere. Here the spouses are bound to a partner whom they perceive at a deep level as hostile and controlling, yet against whom they feel helpless, and toward whom they are driven for protection.

These parents of schizophrenic children tended to identify all perceptions at various levels, while the control parents did not. This apparent constriction in perception, and stereotypy of a hostile world, suggest strongly that these parents were more rigid and inflexible in their appraisal of, and response to, their world.

This would seem to corroborate the postulated differences between normality and mental illness. Kubie [14] has stated this succinctly (page 203):

Whenever the conscious-preconscious alliance is dominant among the operative forces the resultant patterns of behavior, no matter how varied they may be, will have one basic characteristic in common, namely that any repitiveness which that behavior may exhibit with respect to impulse, thought, action, or feeling, or any combination of these, will be flexible, modifiable, satiable, and under voluntary control. A dominant unconscious alliance, on the other hand, whatever its detailed composition, produces behavior that in this specific respect will have precisely opposite characteristics; it will be repetitive, obligatory, insatiable, and stereotyped. Preponderance of the unconscious system predetermines the stereotyped and automatic repetitiveness that is the sign of the neurotic process.

The close identification of social façade and ego-ideal of the patient-parents in this study, as compared with the controls, seems contradictory to the findings reported by Hillson and Worchel.[15] They noted no significant difference between schizophrenics and normals for this comparison, but a significantly greater discrepancy between the two perceptions for neurotics. It may be that the controls in our study were mainly "neurotic" persons, and/or that our methodologies were not comparing the same variables. The difference in the two groups reported in this study was due to a greater emphasis on domination and strength of the ego-ideal by the patient-parents.

Summary and Conclusions

This study attempts to identify certain personality and characterological traits of parents of schizophrenic and normal children. There are hints that such differences do exist and that they can be detected by this methodological approach. Such suggestive findings can be corroborated by a more extensive project, including more subjects. In addition, it would be important to study another control group of parents subjected to the prolonged severe stress of having children with emotional and/or physical ailments not schizophrenic. These additional

data should shed light on the problem of "feed-back," whereby parental perceptions and behavior are modified by stress. Our assumption in this paper was that the behavior and personality patterns of the children were related at least in part, to the personality of their parents. Our observations were as follows:

1. Five marital couples, 10 parents of autistic children, were compared with six marital couples, 12 parents of apparently normal children, by the interpersonal diagnostic system of personality evaluation.

2. As a group, the patient-parents tended more closely to identify the 32 variables studied, indicating rigidity and stereotypy of perception.

3. Patient-parents showed greater self-deception than did the control parents.

4. On a preconscious level, patient-parents identified "hero" and "other" figures, suggesting some failure of their psychological maturation in the process of differentiation.

5. Patient-parents consciously identified their mothers and their spouses.

These results suggest that this method of personality evaluation can be used in the study of the parents of schizophrenic children and normal children.

The small number of subjects in this pilot study should be augmented by a more extensive project to include a study of "feed-back" investigating control parents of chronically ill children with disorders other than schizophrenia.

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Sensory Deprivation

A Technique for Studying Psychiatric Aspects of Stress

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Introduction

The study of the phenomenon of perceptual and sensory deprivation * is a new development in modern psychiatry. It has long been known that explorers or shipwrecked sailors exposed to a restricted or monotonously repetitive environment for extended periods of time may develop psychotic-like mental states.[1] In recent years it has also been recognized that the technique of "brainwashing" often involves solitary confinement and deliberate impoverishment of the subject's sensory life.[2]

Attempts to establish experimentally the necessary conditions of sensory deprivation in man were first reported from Hebb's laboratory in 1954.[3] Abnormalities in the behavior of animals in isolation were noted by Reisen.[4] In the original and in subsequent studies with human volunteers only a small number of subjects have been tested by any one investigator. There has been disagreement among the workers in the field regarding the significant features of the experimental conditions and the results obtained.[5] We have reviewed the general literature on the subject elsewhere.[6]

Our interest in the subject of sensory deprivation arose from the observation [7] that poliomyelitis patients treated in a tank-type respirator frequently develop psychotic-like symptoms. Clinical evidence ruled out toxicity or metabolic changes as the cause of these symptoms. We decided to test the hypothesis that the conditions of life in a tank-type respirator might be sufficient to produce the mental abnormalities. We found that some human volunteers also experienced psychotic-like symptoms, but that there was a wide variation in the reactions of different patients in the same experimental situation. These findings suggested a method of testing human behavior and human thought processes, one that could be standardized reasonably well and controlled. Observations could now be made with relevance to the following: (1) sensory deprivation as a form of stress; (2) experimental production of psychotic-like states without the use of drugs; (3) effect of sensory deprivation on learning and performance tasks; (4) effect of imposed sensory structuring upon the sleep-wakefulness cycle; (5) "Brainwashing."

In our initial experiments we have been particularly concerned with sensory deprivation as a form of stress. In subsequent

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* This phenomenon has been referred to in the literature in a variety of ways. Though we believe the term "perceptual and sensory deprivation" best describes our technique, in this paper, for convenience, the term "sensory deprivation" will be used alone.

work we plan to investigate and report on the other problems.

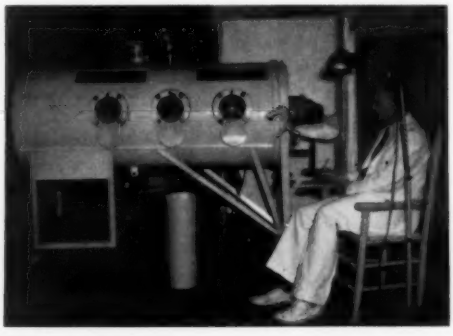
Procedure

Normal men were used as volunteers for these experiments. They were medical, dental, or graduate students or medical house officers. They were recruited through the offer of pay per hour for the duration of the experiment. Each experiment was begun on a Saturday for the convenience of subjects and observers.

The subject was placed in a tank-type respirator with a specially built mattress designed for the better support and comfort of the subject's back. The vents of the respirator were left open, so that the subject breathed for himself. His arms and legs were placed in comfortable but rigid cylinders to inhibit movement and tactile contact. The subject lay on his back and was unable to see any part of his body. The motor of the respirator was run constantly, producing a dull, repetitive auditory stimulus. The room admitted no natural light, and artificial light was minimal and constant. A screen, placed about the respirator, permitted observation of the subject, but the subject could see only a small area of ceiling and screen. The subject was dressed in a loosely fitting hospital gown (Fig. 1).

Subjects who agreed to participate in the experiment were told: "This is a study to see what happens to normal people when they are placed in a tank-type respirator but breathe for themselves. We would like you to lie on your back in the respirator with your arms and legs in cardboard cuffs and to move as little as possible. The experiment will last up to 36 hours unless you desire to terminate it earlier. An observer will always be present, but you will not be able to see him and he will not speak to you. If he leaves the room, it will be only for a minute or two. Your physical needs will be taken care of, and any of your reasonable requests regarding food, water, elimination, or comfort will be satisfied."

Fig. 1.—The tank-type respirator in the experimental setting.



During the experiments, observations and recordings were made of everything the subject said and did. Subjects were fed at intermittent and irregular intervals designed to meet nutritional needs without providing sensory time cues. Bedpans or urinals were given on demand. When the subject requested to be let out, the experiment was ended.

At the end of the experiment the subject was removed from the respirator and was interviewed at length. Emphasis was placed on his feelings, fantasies, preoccupations, and experiences of time and space orientation during his period in the respirator. The material verbalized while in the respirator was brought up by the interviewer in detail.

All subjects were given the following psychological tests within several weeks after they completed the experiment: (1) Murray Thematic Apperception test, (2) Edwards Personal Preference Schedule, (3) Minnesota Multiphasic Personality Inventory, (4) Rotter Sentence Completion test. The clinical assessments from the psychological data were made independently of all other data in the study.

In three subjects (5, 6, and 11) an electroencephalogram was taken intermittently throughout the experiment; electrode placement was done at the beginning of the experiment.

Results

Seventeen men ranging in age from 24 to 31, were the subjects of this study. They stayed in the respirator from 1 hour 38 minutes to 36 hours (Table 1, Fig. 2). Although all the subjects ostensibly entered the experiments because of the monetary reward, in the interviews five subjects reported that their primary motivation was to test themselves to see how they would perform

TABLE 1.—*Data on Seventeen Normal Subjects Placed in Respirator*

Subject	Age, Yr.	Motivation for Entering Experiment	Time in Tank, Hr. + Min.	Reason for Leaving
1	26	Money	19:55	Somatic
2	25	Money	17:45	Anxiety
3	25	Test self	36:00	Completed time
4	28	Money	36:00	Completed time
5	31	Test self	6:50	Somatic
6	28	(1) Money; (2) rest	10:00	Somatic
7	24	Test self	5:23	Somatic
8	25	(1) Money; (2) rest	12:55	Somatic
9	24	(1) Money; (2) curiosity	12:00	Completed time
10	31	Money	36:00	Completed time
11	25	Money	5:35	Anxiety
12	28	(1) Test self; (2) money	2:30	Anxiety
13	26	Test self	1:38	Anxiety
14	29	Aid science	15:40	Somatic
15	28	Money	36:00	Completed time
16	29	Money	36:00	Completed time
17	26	Money	29:45	Somatic

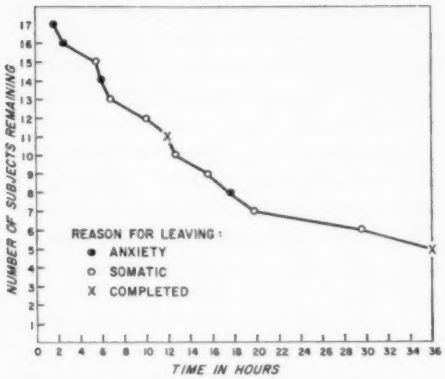


Fig. 2.—Duration of time subjects remained in respirator and reason for leaving.

in the experimental setting. One said that he wanted "to help science." In addition to their primary motivation, five said they thought the experiment would provide a good opportunity to relax. Five subjects were able to remain in the respirator for the agreed 36 hours, and one, for an agreed 12 hours. Four subjects terminated the experiment because of anxiety and panic, and seven, because of somatic complaints (backache or headache). Of the four subjects who developed panic, 2 tried to release themselves forcibly from the respirator. (Fig. 2).

All subjects made errors in judgment of time while in the respirator. The errors in judgment at the end of the experiment are shown in Table 2. It may be noted that those subjects who remained in the respirator 36 hours made a minimum of error, whole those who left earlier made greater errors.

Motor Activity.—The degree of motor activity of the subjects while in the respirator was as follows: Three showed little or no apparent movement; three, slight movement, and six, moderate movement; five were hyperactive.

Verbalization.—The amount of verbalization was as follows: Two subjects said nothing; six produced infrequent speech; four, moderate amounts of speech, and five were verbose.

The total number of somatic references (complaints of physical discomfort) is shown in Table 3. They varied from 1 to 40. Because of the varying lengths of time the subjects stayed in the respirator, the somatic references were also computed in number per hour.

Both in motor activity and in speech the subjects varied over the entire range of possible responses.

Concentration.—Most subjects reported that while in the respirator they lost the ability to concentrate on specific ideas. This loss was characterized by an increasing difficulty to think through abstract problems or do mental arithmetic.

Other Mental Experiences.—Verbal content was categorized somewhat arbitrarily into six groups, as follows:

1. Analogy: Any experience which was reported with the preface, "it feels like" or

TABLE 2.—*Error in Time Estimation at End of Experiment*

Subject	Time in Tank, Hr.	Hours Error	$\frac{\text{Error}}{\text{Time in Tank}} \times 100$
1	19.9	−10.0	50%
2	17.8	+ 3.5	20
3	36.0	+ 1.0	3
4	36.0	+ 2.0	5
5	6.8	− 3.0	44
6	10.0	+ 0.5	5
7	5.4	− 3.0	56
8	12.5	+ 1.0	8
9	12.0	− 3.5	29
10	36.0	− 0.12	0.3
11	5.6	− 2.0	36
12	2.5	− 0.5	20
13	1.6	+ 0.8	46
14	15.7	+ 9.0	56
15	36.0	− 1.0	3
16	36.0	+ 1.25	4
17	29.7	+ 2.5	8

TABLE 3.—*Somatic References During Respirator Experience*

Subject	Time in Tank, Hr.	Total Number of References	References Per Hour
1	19.9	10	0.50
2	17.8	40	2.39
3	36.0	7	0.19
4	36.0	11	0.30
5	6.8	1	0.15
6	10.0	13	1.30
7	5.4	6	1.15
8	12.5	3	0.24
9	12.0	2	0.17
10	36.0	23	0.64
11	5.6	2	0.35
12	2.5	3	1.30
13	1.6	2	1.25
14	15.7	1	0.06
15	36.0	2	0.06
16	36.0	4	0.11
17	29.7	10	0.34

"as if." (Example: "This feels like being on a train in a Pullman car.")

2. Daydream: Any thought the subject reported concerning events in the past or anticipated in the future. (Example: "I've been thinking of a trip I took by boat when I was a little boy.")

3. Fantasy: Mental phenomena reported as though actually occurring but with recognition of their unreality. (Example: The subject reported he imagined and actually felt as though he were making love to an attractive girl.)

4. Pseudosomatic Delusions: A feeling of change in body sensation preceded by an "as if." (Example: "It feels as if my hands are separated from my body.")

5. Illusion: A misinterpretation of a perceptual experience. (Example: A spot on the ceiling was reacted to as though it were a spider descending toward the subject.)

6. Hallucination: A sensory experience without basis in reality. (Example: "I see a group of soldiers dressed like George Washington standing on a cliff. Now they've changed to a bunch of cows! The colors are bright orange and black.")

Summary: Fifteen of the subjects reported analogies; 11, daydreams; 6, fantasies; 5, pseudosomatic delusions; 5, illusions, and 3, hallucinations. A tabulation of these mental experiences for each subject may be seen in Table 4.

TABLE 4.—*Mental Experience Reported by Subjects*

Subject	Analogies	Daydreams	Fantasies	Pseudosomatic Delusions	Illusions	Hallucinations
1	×	×	×			
2	×			×		×
3	×	×	×	×	×	
4	×			×		
5		×			×	
6	×	×				
7	×	×	×			
8	×	×			×	
9	×		×		×	
10	×					
11		×				
12	×					
13	×			×		×
14	×	×				
15	×	×	×			
16		×	×	×	×	×
17	×	×				
Total	14	11	6	5	5	3

Elimination.—Two subjects suffered from acute urinary retention with marked bladder distention. Most subjects were unable to void the first time they attempted to do so. No subject attempted to defecate.

Psychological and Statistical Findings.—In view of the exploratory nature of the present study and the difficulty of formulating a priori hypotheses about the relationships of psychological test scores to performance in this experimental situation, it was decided to forego such hypotheses. Instead, we examined a wide range of scales for their relationships to the length of time subjects remained in the respirator. These relationships were estimated by the use of Spearman's rank order coefficient of correlation corrected for tied ranks. It was further decided that, owing to the preliminary nature of the study and the limited controls in the procedure, a finding would be considered significant whenever $P<0.10$. For the pilot purposes of this investigation, we were more concerned about rejecting a true hypothesis than we were about accepting a false one. We shall describe only the significant and near-significant relationships found.

Of the 16 correlations computed for MMPI scales against time in the respirator (including two scales which combined scores on other scales), none was found to be significant. On the Edwards test, three scales met our criterion, and one fell short of doing so by a very small margin. The scales found to be related to time in the respirator were the following, and these will be presented, along with excerpts of the definition of these scales given by the author in his manual for the test [8]:

1. Need Exhibitionism: "Need to say witty and clever things, to be the center of attention, to say things just to see what effects they have on others." This scale was found to be negatively related to stay in the respirator at $P<0.01$.

2. Need Affiliation: "Need to be loyal to friends, to make as many friends as possible, to do things with friends rather than alone,

to form strong attachments." This scale was positively related to stay in the respirator at $P<0.10$.

3. Need Succorance: "Need to seek encouragement from others, to have others be kindly, to have others be sympathetic and understanding about personal problems, to receive a great deal of affection from others." This scale correlated positively with time in the respirator at $P<0.10$.

4. Need Nurturance: "Need to help friends when they are in trouble, to treat others with kindness and sympathy, to be generous with others, to show a great deal of affection toward others." This scale correlated positively with time in the respirator at just below $P=0.10$.

In addition to the above relationships, the following were also found to be significant: Time error per hour scores were found to be negatively related to length of stay in the respirator at $P<0.01$. This meant that the distortion in time estimates (divided by the number of hours in the situation) was significantly lower for the subjects who remained longer. The number of somatic complaints per hour was also related negatively to time in the respirator at $P<0.10$. This indicates that people who stayed in the respirator longer had the lower rate of somatic complaints. Finally, we observed that rate of complaints (somatic complaints per hour) was significantly and negatively related to Taylor Anxiety scores obtained from the MMPI items. This relationship was significant at $P<0.10$, and suggests that the greater the manifest anxiety level, the lower the rate of somatic complaints.

Report of Cases

The following two cases are presented to illustrate some of the behavorial and psychological phenomena observed in our subjects.

CASE 1 (Subject 2).—A 25-year-old white unmarried dental student remained in the respirator 17½ hours.

He entered the tank at 10 a. m. and immediately complained of neck pain and of feeling as if he were in "a short-necked prison" (*sic*). A few minutes later he said he wasn't sure whether he was awake or asleep and wondered about the purpose of the experiment, complaining that he had not been told what was really the purpose of it.

Within the first hour he began to perspire profusely and continued to do so for the rest of the experiment. At the end of the first hour he tried to amuse the observer by telling a series of jokes. The subject wondered if the observer was still present and decided he could find this out by asking for a drink of water. He then requested water and continued to do so frequently until the end of the experiment.

At 1 hour and 15 minutes after entering, the subject began to describe rapidly changing, vividly colored, three-dimensional scenes which he saw with his eyes closed. Each scene changed as he described it, and the subject paused a minute or two between descriptions. He complained of feeling drowsy during this time. "I see a pool of water, a roll of toilet paper with a nail at the end of it sticking in the water. Hallucinations, I guess."

At 1 hour and 33 minutes he said: "Now I see a beautiful technicolor sunrise over a lake, nice ripples, three dots, must be a moon, three dots; dark on the other side of the lake. A bunch of Indians on the shore; they have headdresses, now two feathers apiece." A few minutes later he said, "I hope you've got a lot of paper to take this down. I must be going nuts." He then laughed and continued: "I see an enamel table of white metal with a ball over it. Next I see a fireplace. Through the door there is a knight in armor. I see a spoke shoot out below his waist, all metal, coiled; it shoots from a can." These productions were made over a 45-minute period, during which time the subject continued to complain of perspiration and pain in his neck.

At two hours the subject dozed off briefly; and when he awoke, he began to move about in the tank. He removed his extremities from the containers. From two and one-half to seven and one-half hours the subject complained frequently of pain in his left side, which he associated with being constipated, and tried to maintain contact with the observer by (1) frequent requests for water, (2) asking what the observer was doing, and (3) wondering how long he, the subject, could stay in the respirator. During this period motor activity was marked.

At seven and one-half hours the subject said he would like to leave the tank, and the observer replied that he could if he was acutely uncomfortable. The subject decided, "I can stand it."

The subject voided for the first time nine and one-half hours after entering the respirator. Verbalizations began to diminish about this time, but the productions continued to have the same content as before. Nine and one-half hours after entering, the subject was oriented for time. At 10½ hours

he said: "My left side is gone." The subject slept most of the time until 14 hours and 54 minutes, when he said: "Well, to tell you the truth I am stuck here. Am I alone?" He was unable to estimate the time and sounded very anxious.

The subject fell asleep 16 hours after entering. At 3:30 a. m. (17½ hours after entering) he began to punch and shake the respirator. He pulled his head into the tank, extended an arm through the neck opening, and tried to release the hooks holding the respirator closed. He was agitated; his eyes were full of tears, and his voice was shaking. He thought it was seven a. m., when it was actually 3:30 a. m. The subject was removed from the tank. It took him 15 minutes to calm down.

In the subsequent interview the subject complained that he had been promised that an observer would be with him at all times. He had awakened, asked for a drink of water, and, hearing no response, had said to himself: "If you're not here, I'll get it myself."

The subject has been preoccupied with bowel function for many years, particularly since his father died, a year prior to the experiment, with obstipation as a terminal symptom of congestive heart failure and uremia. The subject often has back pain when he sleeps on his back. He normally perspires a great deal and drinks large amounts of water. He has a vivid imagination and can make up stories and poems with facility. As a child, after disagreements with his playmates, he would find solace in reading books.

After awakening from the sleep which followed his visual experiences, the subject felt: "Things were different. I wasn't at ease in the tank. I might have continued seeing things if you were still there. Then I began to feel physically uncomfortable, my back hurt. . ." Several times during the interview the subject apologized for terminating the experiment and asked how well he had done in comparison with other volunteers.

Summary of Case 1.—The subject responded to the stress of the experiment with (1) early onset of somatic complaints, perspiration and thirst, which persisted throughout the experiment; (2) attention-getting devices, by which he attempted to maintain contact with the observer; (3) a series of vivid, brightly colored, three-dimensional visual images, which the subject knew were not real, occurring 1 hour and 15 minutes after entering the respirator; (4) mounting anxiety, which became increasingly difficult to control, indicated by distortion in time judgment, pseudosomatic delusions, and, finally, panic.

Clinical Impression.—The subject is an emotionally labile person with a great need to please others. He is ambitious and seems to have some identification with his mother. His defenses against anxiety are inadequate. He readily utilizes fantasy, autonomic symptoms, and somatization.

Clinical Assessment from Psychological Data for Case 1.—The subject assumes a "hail fellow well met" approach to the environment with an overtly jocular, confident manner. He conforms to all demands and sometimes expresses hostility through either an overly conforming, literalistic interpretation of tasks confronting him or through hostile joking. He tends to deny the existence of all problems and difficulties in an omnipresent optimism. His record reveals a strong concern with being "normal," and he seems to accept parental values as guides for his behavior, with strong influence of religious themes. The world is frequently divided by the subject into two opposing camps of good and evil, or right and wrong.

The record points, further, to considerable ambition and drive for achievement. He expresses a sense of deprivation by adult authority and a feeling of martyrdom for the sake of his peers. This latter may be related to strong competitiveness and possible sibling rivalry.

His response to failure is to externalize responsibility and blame others. Under stress he reveals an extremely elaborate fantasy life, in which things are not at all what they appear to be on the surface and there is suspicion of the trustworthiness of others. While his thinking is often intricate, he is able, when pressed, to account for his ideas. Difficulties are resolved in fantasy by magical resolution and denial, which reveal a child-like conventionality.

CASE 2 (Subject 15).—The subject, a 28-year-old married house officer, remained in the respirator the full 36 hours of the experiment.

He entered the respirator at 10 a. m. After five minutes he said: "I thought this was going to be snappy, but it is going to be more trying than I thought." During most of the first two hours he remained relatively immobile and appeared to be asleep. In the third hour he commented about the

change in the sound of the respirator, began to turn spontaneously, and tapped on the side of the tank. He spoke little during the third and fourth hours.

In the 5th through the 10th hour the subject moved a great deal, ate a meal, and voided. Verbalizations were infrequent. From the 11th to the 17th hour the subject slept, moaning in his sleep and turning frequently. At 17 hours (3 a. m.) he awoke, stated that he was cold, and said, "Why can't I have a sheet?" He fell asleep again and awoke at 19 hours. He said: "I almost panicked early this morning before I asked for the sheet. I pushed against the sides of the tank. It was very hot." At this time the subject was fed, and he voided again.

From the 19th to the 22d hour the subject slept intermittently. He said little. Upon awakening, he whistled, sang songs, and turned on his side frequently. At 24 hours he reported: "I don't feel so bad; I feel better than when I went in. My back is killing me, but it really isn't so bad because I can move, I can turn over."

During the remaining time in the respirator he slept intermittently and moved frequently, changing position from side to side. Toward the end of the time in the respirator he began to use profanity and kicked and tapped against the side of the tank. At the time of removal, 36 hours after entering, he said: "I don't think a hell of a lot will happen as far as my own experiences are concerned, just that one time yesterday morning."

In the subsequent interview the subject's first reaction was: "What a snap, even the question of time was not difficult. I don't think I ever got to the point of panic except when I couldn't move around. Early this morning, just before you put the sheet on, I was moving around banging things. I wanted to push everything; I felt closed over. Something that really bothered me was my loss of sense of time. I tried to judge time by fullness of bladder and meals. I sort of got fed up being in the tank. I knocked on the walls. Whenever it got unbearable, I whistled."

The subject had several daydreams, which occupied his mind for a great deal of time. They were concerned with pleasant past events, such as working in his garden and playing softball. He dwelt particularly on the time he played softball on an Army team and traveled across the country to participate in a tournament. He did not think of particular persons in his life but, rather thought of general events and situations. He amused himself by singing off-color songs and whistling. He kept thinking of the goal, i. e., completing the experiment and receiving his payment. In general, he attempted to make the best of things regardless of the discomfort. He felt his greatest problem was his loss of sense of time.

Asked about volunteering for another such experiment, the subject replied: "It's damn monotonous. I hesitate to answer yes; I couldn't stand it to lie on my back for a long period of time. I was wondering what keeps a polio patient's sanity. If I had to stay in for weeks, it would severely test my sanity."

Summary of Case 2.—The subject responded to the stress of the experiment with (1) marked motor activity, and verbal behavior, such as singing; (2) concentration on the goal of release and payment, combined with a resignation to tolerate the situation to the best of his ability; (3) preoccupation with daydreams of past pleasurable physical activity; (4) one episode of disorientation, confusion, and near-panic, which the subject was able to tolerate.

Clinical Impression.—The subject is a well-integrated mature person, who is strongly motivated to succeed and able to tolerate stress and anxiety.

Clinical Assessment from Psychological Data for Case 2.—This subject shows a primary concern with achievement and a strong ambitious drive. Although feeling that the path to achievement may be fragile and expressing some uncertainty about his ability to reach his goals, he recognizes some of the unreal aspects of his strivings. He, further, seems involved in modifying some of his unrealistic standards. While manifesting some tendencies to impulsive action, these appear to be under control.

The subject's interests and values have a strong intellectual quality with a concern for ideas, values, and matters artistic, in which he reveals markedly critical opinions. The record shows a sensitivity to threat, concern with not being "taken in," and the arousal of vengeful hostility in circumstances where he is fooled. He assumes a cynical, critical attitude toward his peers and their "false values." On the other hand, he has a great respect for paternal authority and confidence in its wisdom. He expresses a generalized need for and appreciation of family in particular and other people in general. His fantasy life appears to be minimal and appropriate to his situation.

Comment

Most techniques for the experimental production of stress involve such stressors as increased physical stimuli, pharmacological agents, and psychological tasks. In contrast, sensory deprivation as a form of stress differs from these techniques in that physical stimuli are decreased, pharmacological agents are not used, and, psychologically, there is a reduction in perceptual, conceptual, and social stimuli.

We should like to discuss the methodology employed in this study in some detail because of the variable results reported in the literature. The selection of subjects is of first consideration. We employed male medical, dental, and graduate students and medical house officers because they were available, had relatively high I. Q.'s, and could verbalize readily. Though we had several refusals by persons who were approached as possible subjects, there was only one actual refusal after a man had initially accepted. Thus, it is clear that we have not recruited a random sample.

Monetary reward was used as a means of recruitment because of its efficacy in recruiting and its utilization in other studies. While money was the ostensible reason for volunteering, several of our subjects gave other motivations for their participation. It is possible that the desire to test one's self or to "aid science" may be related to some of the results obtained, in that subjects with such desire may be prone to reporting unusual experiences. However, only 3 of the 6 subjects who participated for reasons other than monetary reported disturbances in reality, while 5 of the 11 subjects who presumably participated solely because of monetary reasons showed distortions of reality. Distortion of reality, therefore, was not confined to the group who desired to test themselves.

We have attempted to define and control the perceptual and social variables in the experimental situation. However, it must be considered that the respirator situation imposes a psychological stress on a person in isolation because of the novel experience for the subject. This may well be another aspect of psychological stress. Additional psychological stress may occur as a result of inability of the subject to view his own body. These factors, both independent of sensory deprivation, should be considered in interpreting the results obtained.

When we attempt to correlate the psychological characteristics of our subjects with the length of time they were able to remain in the respirator, we find an interesting result. Those subjects who stayed in the respirator longest were just those who expressed greater need for being with other people. The psychological tests indicated that they desired more contact with people, were more dependent upon them, were more emotionally giving to them, were less exhibitionistic, and were genuinely more related to others. In addition, they seemed to be less complaining, perhaps adapting more readily to physical discomfort. Those who complained less were those who on tests reported more manifest anxiety. This finding tends to support the view that somatization may be a means of binding anxiety. Finally, the data suggest that those subjects who stayed in the respirator longest were those who showed least distortion in time judgments. It appears that the ability to remain in the respirator is a function of the adequacy of reality orientation and that sensory deprivation acts as a stressor precisely because it jeopardizes the subject's hold on external reality.

The techniques thus far employed by others in the production of sensory deprivation fall into three general categories:

1. Attempts to reduce the absolute level of intensity of all physical stimuli, as exemplified by Lilly's [9] reports of his own experiences under such conditions.

2. Attempts to reduce the patterning of stimuli, as reported in the studies of Vernon and Hoffman [5] and by Hebb and his associates.[3,11-12]

3. The imposed structuring of stimuli as reported in clinical studies with poliomyelitis patients.[7]

Our present studies utilize imposed structuring of stimuli as the essential methodological approach, though elements of the other categories are present. In imposed structuring of stimuli, the subject receives essentially constant physical stimuli, which are both unvarying and repetitive, yet are not reduced in absolute level of intensity. Form and pattern discrimination are limited but not completely abolished.

The previous studies of sensory deprivation report the general behavior of subjects as determined by the observation of responses and by task performance tests. The concept of sensory deprivation as a stress situation has not been developed. However, certain major findings are present in most previous studies and are supported by our data. These are (1) the inability of most subjects to tolerate or adapt to the stress of sensory isolation; (2) the subjects' increasing need for and attempts to obtain extrinsic physical and social stimuli; (3) the progressive failure, in certain subjects, of reality contact with the emergence of pathological thought processes and behavior.

It is apparent that sensory deprivation can produce major mental and behavioral changes in man. Its use as a stressor agent and for the production of psychotomimetic effects may prove more "natural" than the pharmacological and physical methods currently used. However, the same exactness in examination of criteria is necessary for its understanding.

Summary

As a means of inducing stress, 17 normal male volunteers were exposed to perceptual and sensory deprivation through the use of a tank-type respirator for periods up to 36 hours. Though there was considerable variation in individual responses, all subjects showed impaired ability to concentrate, distortions in time judgment, and degrees of anxiety. Eight had pseudosomatic delusions, illusions, or hallucinations. A variety of psychological tests were given, and the results were correlated with the behavior in the experimental situation. Two cases are described in detail. The findings are discussed in relation to pertinent psychological and psychiatric literature.

Drs. Fortunato Castillo, Robert Duncan, and Hans Preuss, psychiatric residents at the Boston City Hospital, 1956-1957, and Dr. Egbert Mueller, resident in psychiatry as the Massachusetts General Hospital, assisted in the observation of subjects involved in this study.

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Books

BOOK REVIEWS

Role Relations in the Mental Health Professions. By Alvin Zander, Arthur R. Cohen, and Ezra Stotland. University of Michigan, Ann Arbor, Mich., 1957. Price, $4.50. Pp. 211.

With the rapid growth of mental health facilities during and since World War II the concept of the "mental health team" has emerged to describe the collaborative efforts of psychiatry, clinical psychology, and psychiatric social work. New roles and role relationships are evolving which in some respects have led to mutual satisfaction, although in others to conflict and strain. This volume is a study of the role relationships among the professions in today's psychiatric clinic, focusing not on the product of the collaborative work but on the attitudes, expectations, and feelings of the members of the various professions in their relations with one another.

It is not surprising that persons professionally concerned with the satisfactions and frustrations of social interplay in the lives of their patients should turn their interest upon themselves and try to view with some detachment their own social transactions. Yet such concern with the social dynamics within which mental health work is done has only in the recent past become a self-conscious interest of the mental health professions. It still takes the relative outsider—in this case social psychologists—to view the behavior of mental health workers as itself worthy of scientific and systematic concern. In this respect, the present volume falls into an important new area which has concerned itself with such problems as the psychiatric hospital as a social institution and multidisciplinary clinical or research groups as proper objects of study.

The study of role behavior stands at one of the more important boundaries between the social and the psychological sciences. For many years role has been the concern of sociologists, who in general have viewed it in terms of the larger social institutions which create and sustain role patterns. More recently, however, role has been utilized as an organizing concept in the psychological study of social behavior. In the authors' definition, a role "is a set of behaviors which an individual is expected to perform. In the professional role such behaviors concern task functions, responsibility relations, and normative relations, which are expected of an individual by relevant others. These expectations of a role occupant may be called prescriptions for the role." Roles interlock, and the prescriptions for each must be described in terms of the prescriptions for the others. As a member of a professional group the individual shares the aspirations, goals, and values of his group and must conform to its standards.

Coming from the Research Center for Group Dynamics of the University of Michigan, the present study is in the tradition of Kurt Lewin and the later workers in group dynamics, although strongly influenced by the more recent thinking of Theodore Newcomb. Consequently, it focuses primarily on the psychological aspects of role behavior—the perceptions, expectations, feelings, values, and the like held by role occupants in their interrelations. Central among the concepts used is the security experienced in the expectation that individual and group needs can be gratified in given relationships with other roles. Derived from such expectations are the observed feelings of esteem, conflict, and rivalry. Quite aside from its value to the specific understanding of the mental health professions, the book makes a more general contribution to the psychology of role behavior. The study could as well have been done on any other combination of groups interlocked in a social system, and, indeed, many of the principles found here are of the generality necessary to understand role behavior in many settings.

The aspects of role behavior studied by Zander, Cohen, and Stotland fall readily into two major classes. On the one hand, there are the variables which describe the prescribed role relationships and include the perceived power to influence, the acceptance of such power, the frequency of professional contacts, professional knowledge and skills, satisfaction from providing counsel for others, satisfaction with interrole relations, and prestige in one's own profession. Related to these, in the nature of dependent variables, are such factors as attitudes of admiration and esteem, attitudes indicating either the use or the receipt of solicitous behavior, attitudes indicating either the use or the receipt of encroachment or hostility, stereotypes about the other groups, and disposition to communicate with other groups.

The data of the study consist of individual interviews with roughly 160 members of each of the three groups chosen from among active workers in clinical settings providing opportunity for interaction, mainly in the larger American metropolitan areas. All of the participants were trained to the standards of their respective professional organizations, and were associated with a variety of agencies, including University and private hospitals and clinics, Federal and state hospitals, clinics and schools, and independent social agencies. The authors take pains to describe carefully their sample and methods, and to give detailed information about the actual interview responses.

What emerges is an intriguing—though often familiar—picture of the interplay of the three professional groups. "The mental health profession provides a hierarchical society of persons who commonly value close teamwork. Psychiatry is at the top of the triangle, while clinical psychology and psychiatric social work are at the bottom points." Psychiatrists have the superior position and with it the expectation that they are to supervise the work of the other two groups. All three groups share this perception of the status difference. Thus, asked "if you had it to do all over again," all of the psychiatrists choose psychiatry, while only about two-thirds of each of the other two groups would again choose their present profession, the remainder preferring psychiatry. However, the relationship of psychiatrist-social worker differs considerably from the relationship of psychiatrist-psychologist.

In the main, psychiatrist and social worker are symbiotically related, each perceiving himself in much the same terms that the other perceives him. Social workers accept the difference in power, and view themselves as an auxiliary profession. They are eager to be liked and respected by psychiatry. They believe that psychiatrists have more knowledge and skills than they; although as a group they desire somewhat more power, they are generally satisfied in the interrole relations. Functions are clearly delineated and their complementarity clearly defined. Both groups accept this placement as proper and hold attitudes which maximize the possibility that the groups will supplement each other. "In short, a crucial basis of the social workers' satisfaction in relation with psychiatrists is the acceptance of their traditional position as helpers and assistants." Paralleling this, the psychiatrists feel no need to increase their influence over social workers, feel little concern about encroachments, value professional contacts with social workers, and in general see their skills as supplementary in the work of the psychiatric clinic.

By contrast, the relationship of psychiatrist and clinical psychologist is less well defined and contains more strain within it. At the outset, the two groups perceive differently the functions properly included under "clinical psychologist." The psychiatrist views the role as distinctly more limited, with a central focus on psychometrics, while the psychologist sees his potential contribution ranging over a decidedly broader area of clinical service. Consequently, the psychologist is more likely than the social worker to feel that he is being deprived and to resent the power imbalance, though sharing with the social worker the wish to be admired and respected by psychiatry. The psychiatrist, in turn, sees the psychologist as a potential competitor, and views him as encroaching upon psychiatric functions, though at the same time admitting greater respect for the psychologist's knowledge and skills than for the social worker's. Thus, when asked what their second choice would be, had they again to choose a profession, virtually all psychiatrists said psychology. There is mutual admiration, and apparently a sincere desire for improved relations, but in the present situation strain, uncertainty, and some mutual fear. The relationship of psychiatrist-psychologist is, of course, more recent than that of psychiatrist and social worker and, unlike the latter, is based on male-to-male rather than male-to-female transactions. Interesting in this respect are some separate analyses of the role behavior of female psychologists toward psychiatrists. This subgroup turns out to be neither like the social workers nor quite like their male co-professionals. Like male psychologists, they perceive the same frustrations and also resent the lack of power, but are far less willing to do battle. Thus, it would seem that the professional interrole relations are only in part derivatives of the sex role relations common to our society generally.

Four major themes emerge in the psychiatrists' attitudes toward clinical psychologists. The psychiatrist realizes that he has greater power than the psychologist; he respects the ability of the psychologist; he believes that psychologists should have greater influence, though hardly to the same extent as do psychologists; and he goes along with psychologists in not being strongly satisfied with the existing relations between the two groups. The psychiatrist recognizes the aspirations of the other profession, but is uneasy about the degree to which these

can be gained without constituting a loss to his own group. "To the psychologists, the psychiatrists are gatekeepers. To the psychiatrists, the psychologists are challengers."

Since the interaction between social worker and psychologist is derived from the relationship each has with psychiatry, it is not surprising that there is relatively little concern within each profession with the other's function. There is mutual respect, and generally satisfaction, in the interrole relations, although each feels at least equal or superior in knowledge to the other. Neither profession sees the other either as a potential source of reward or as a threat or barrier to its aspirations. Instead, each is more concerned with the relation of the other to psychiatry. The social worker shares the psychiatrist's definition of the psychologist's role, more limited than the psychologist's own. What emerges, simply, is that these professions have each developed its own role relations with psychiatry and their contacts with each other are generally tangential, although personally satisfying. There is neither conflict nor any great need for collaboration between them.

This study organizes and adds to knowledge of interrole behavior in the three mental health professions; its importance is increased because these findings are viewed in terms of more general social processes. However, for a more complete understanding of the current situation or, more importantly, for predicting or planning the future of the three professions in their joint contributions to the field of mental health, certain aspects of the problem are insufficiently treated.

1. Present role relations should be viewed in historical context. The mental health field has been evolving rapidly, with roles formulated and altered in relatively brief periods. Prior to stable role definitions there is likely to be uncertainty and conflict. Perhaps the greater friction between psychiatrist and psychologist, compared with psychiatrist and social worker, reflects the shorter period of evolution.

2. The role relations described should be understood in terms of the competing role behaviors with relevant others outside the mental health field. Each of the professions extends outside the mental health field, and each member consequently holds overlapping roles, with their associated standards and values. These, in turn, are in transition, and much of what emerges in the behavior of the mental health professions toward each other may have its important determinants outside of the mental health area, narrowly defined. The psychiatrist is at one time "psychiatrist," with its role prescriptions, and at the same time "physician," with its definitions. As the role of psychiatrist changes—for example, with the development of a dynamic psychiatry focusing more on psychological than on physiological processes—the greater is the potential conflict between the psychiatrist and the physician role and the greater the need for integrating the disparate requirements of the two role models. Similarly, many clinical psychologists harbor within them the competing role models involving behaviors and values appropriate to clinical functioning in the psychiatric setting ("clinical psychologist") and derivatives of the older prescriptions of the traditional academic setting ("psychologist"; "scientist"). Not only can much of the behavior of the two professions toward each other be better understood in the light of the conflicts within each, but some of the directions of future role relations can be predicted.

3. The field of mental health, and the relations among the three professions, increasingly extend beyond the team functions involved in the care of psychiatric patients. Quite intentionally, Zander and his colleagues focus their study on the interplay in the clinical situation, inquiring specifically into the functions and perogatives of the groups in diagnosis, therapy, community relations, and other such activities. But the larger field must also include the important tasks of enlarging and communicating the science of mental health itself, and it is in training and research that new role relations are coming into being. Increasingly, psychiatrists are to be found in graduate psychology departments, while psychologists teach in medical school or psychiatric training programs. The interdisciplinary research team, as well as the interdisciplinary training program, depends on the faith that the problems of mental health must be approached from a variety of backgrounds, each group making its unique contributions. Of necessity, these newer relationships involve greater mutual respect and less status difference than existed in the more traditional clinical relationship. It is becoming more commonly recognized that each profession must contribute different areas of knowledge and skills which are entirely supplementary to each other. With this recognition, interrole attitudes have altered. The "scientific" training of the psychologist is an asset and is respected by the psychiatrist in the laboratory, though it may be an annoyance in the clinic. Indeed, there seems to be emerging essentially a new role, not that traditionally of psychiatrist, social worker, or

psychologist, but something which might truly be called the mental health worker, whether researcher, teacher, or clinician. Some years ago Andras Angyal described psychiatry as the application of a science which does not exist. In the development of this science not only these three but other professions among the behavioral and biological sciences will have to work collaboratively in the production of both the substantive and the technical knowledge necessary for more rational clinical practice.

Lastly, one finding of this study draws attention to, and suggests the need for altering, the present hierarchical relation among the professions. It is reported that with increased prestige within one's own profession there is an increased tendency not to desire or seek association with members of the other professions. For psychiatry, this works generally so that the more powerful psychiatrist feels less dependent on other professional groups, though he will more (i.e., than less powerful psychiatrists) value their potential contribution to the mental health field. The more respected psychiatrist realizes his own, and respects his co-workers', competence and feels less threatened by their aspirations. By contrast, however, the persons who have gained prestige in the other, subordinate, professions are less likely (compared with their less prestigeful colleagues) to have respect for psychiatrists, are more likely to prize the unique aspects of their own profession, would prefer to minimize their contacts with psychiatrists, and are over-all less happy with the prescribed role relations. The authors rightfully point out that this set of attitudes characterizes any groups related in superior-subordinate fashion. Thus, the member of a minority social group who gains stature in his own group feels more keenly the actual or implied depreciation in his contact with members of the dominant social group. While this finding points up a general fact of social dynamics, it also highlights an important problem in the continued collaboration of these fields. If one assumes only that the advancement of mental health depends on the best efforts of the most competent persons in all of the professions, it would seem that a continued relationship of dominance might drive out of the joint effort some of the more talented members of the adjunct professions, an event which would be unfortunate in view of the need for further developing the field. The gratification in professional role relations necessary for productive work of the best members of each profession would seem to require some leveling of the power differential. As the authors note, such change cannot come about through the efforts of the weaker members of the team, but must be initiated through a revision of role prescriptions by the most powerful, i. e., psychiatric, member. Since the adjunct professions lack the power to change the role relations, the individual alternative is simply escape, rebellious hostility, or conformity. Each of these courses drains needed talent from the common effort.

The volume reflects the growing pains of the mental health field. It is, however, a sign of maturity that practitioners of behavioral science can turn critical interest on themselves as interrelated social beings and try to describe and understand their social behavior. In the past, advances in the treatment of psychiatric patients have resulted from, first, the increased understanding of inner personal dynamics and, later, the dynamics of patient-therapist relationships. Knowledge of the dynamics of interprofessional relations may represent a further step in the development of psychiatric thinking, and eventually contribute to the improved care of patients. To this end, as well as producing an intrinsically interesting study in social psychology, Zander, Cohen, and Stotland have contributed.

SHELDON J. KORCHIN, Ph.D.

Troubles mentaux au cours des tumeurs intracrâniennes. By H. Hécaen and J. de Ajuriaguerra. Price, 1.5 fr. Pp. 153. Masson & Cie, 120 boulevard Saint-Germain, Paris,[6e] 1956.

This monograph is a study of 439 cases of brain tumor, of which 229 presented mental troubles of one sort or another. The main justification for publishing the study is the fact that all of the patients were examined by the two authors, who have long been attached to the neurosurgical center of the psychiatric hospitals of the Seine.

The symptoms were divided in three groups: (1) confusional demential states, (2) troubles of mood and character, and (3) paroxysmal. The first group includes conditions usually described under such names as obnubilation, torpor, confusion, stupor, and dementia. The second group includes irritability, emotional lability, depressional, hypomanic, and hysterical states. The paroxysmal disorders include hallucinations, hallucinosis, dreamy states, losses of consciousness, psychomotor automatisms, etc.

The detailed study of the 229 cases according to localization occupies 84 pages. This section contains many figures, which it is impossible to summarize here; these are later analyzed by the latest statistical methods.

After a justification of the grouping adopted for the symptoms, the authors study the focal value of the various clinical groups. This necessitated, first, a discussion of possible general pathogenic factors, especially increased intracranial pressure. It was for this reason that, in the statistical study, those cases with choked discs were studied separately from those without choked discs. The authors' material confirmed the general opinion that increased intracranial pressure is not a sufficient explanatory factor even for the confusional demential group, since the mental perturbations are least frequent with the group of subtentorial tumors, which has the highest percentage of choked discs. Nevertheless, they were unable to rule out the hypothesis that intracranial hypertension might play the predominant role at times in precipitating the psychiatric troubles, even in the course of supratentorial tumors.

Concerning a possible role played by the nature of the tumor, the authors note that mental troubles were more frequent with gliomas (60.73%) than with meningiomas (43.26%); but so were the choked discs (gliomas, 73.68%; meningiomas, 60.0%). Their material did not permit them to estimate a possible differential for the various types of gliomas because of insufficient histological control.

Their statistical analysis also gave no support for a possible hereditary factor in development of mental disorder.

All of these factors were, of course, analyzed in particular, as well as in general, according to location, type, mental symptomatology, other symptomatology, etc. The literature on the subject was noted in many relations but was not reviewed exhaustively. As a result of their study the authors conclude:

"According to our study, we may retain, as psychiatric syndromes valuable for neurosurgical practice, the psychic frontal syndrome, with its two predominant aspects (subconfusional excitation with expansivity and irritability, and the akinetic syndrome); the mesodiencephalic syndrome (syndrome of Korsakov, often colored with euphoria, oneirism, or, more rarely, akinetic mutism), and the hallucinatory syndromes for the parietal, temporal, and occipital lobes.

"Naturally, to speak of a focal psychic syndrome does not imply recognition of pathognomonic signs. The procedure has a double sense: on the one hand, the study of the symptoms as part of a clinical whole and, on the other hand, a consideration of the syndrome as part of the general behavior of the patient. It will remain to evaluate the context of each individual case; to study the reactions of the patient to the morbid deficit and the characteristics of his personality; to appreciate, as much as one can, the quality and mass of the lesion by clinical or paraclinical examinations (choking with exudates and hemorrhages, diffuse neurological symptomatology); to take account, finally, of rapidity of evolution, in particular of temporal or cerebellar herniation.

"If one does not take account of these conditions, none of the clinical pictures retained, even were it statistically valid, permits one to affirm absolutely such or such a localization.

"Besides the practical interest of these conclusions, we realize that we should draw also some theoretical conclusions. They are, moreover, implicit in our diagnostic discussion. But the tumor material is liable to too many criticisms for the results of such investigations to validate or invalidate hypotheses concerning cerebral localization. The findings thus gathered keep their value, nevertheless, when one compares them with other anatomicoclinical or experimental data."

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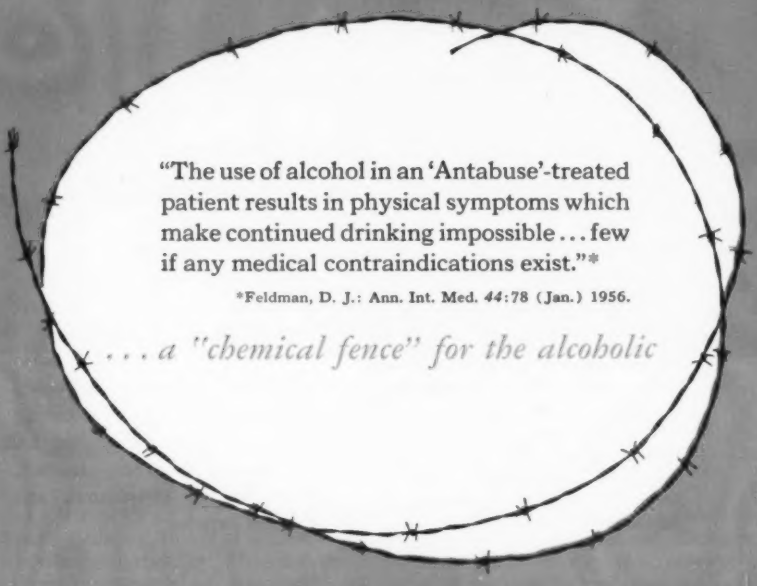

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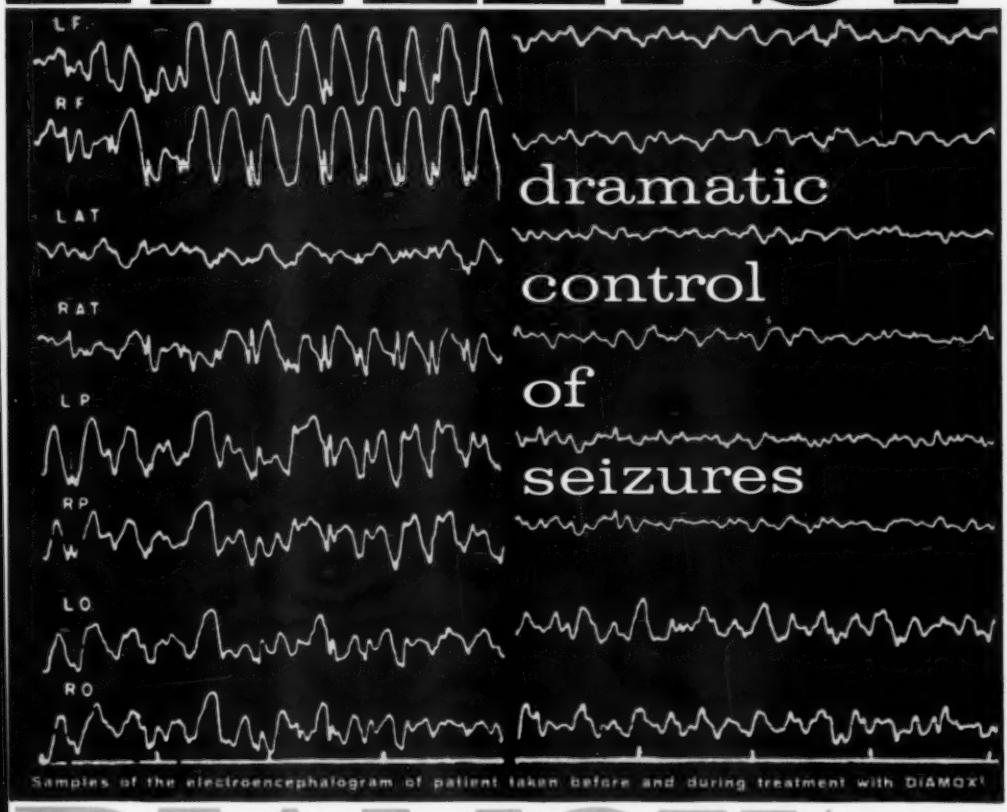

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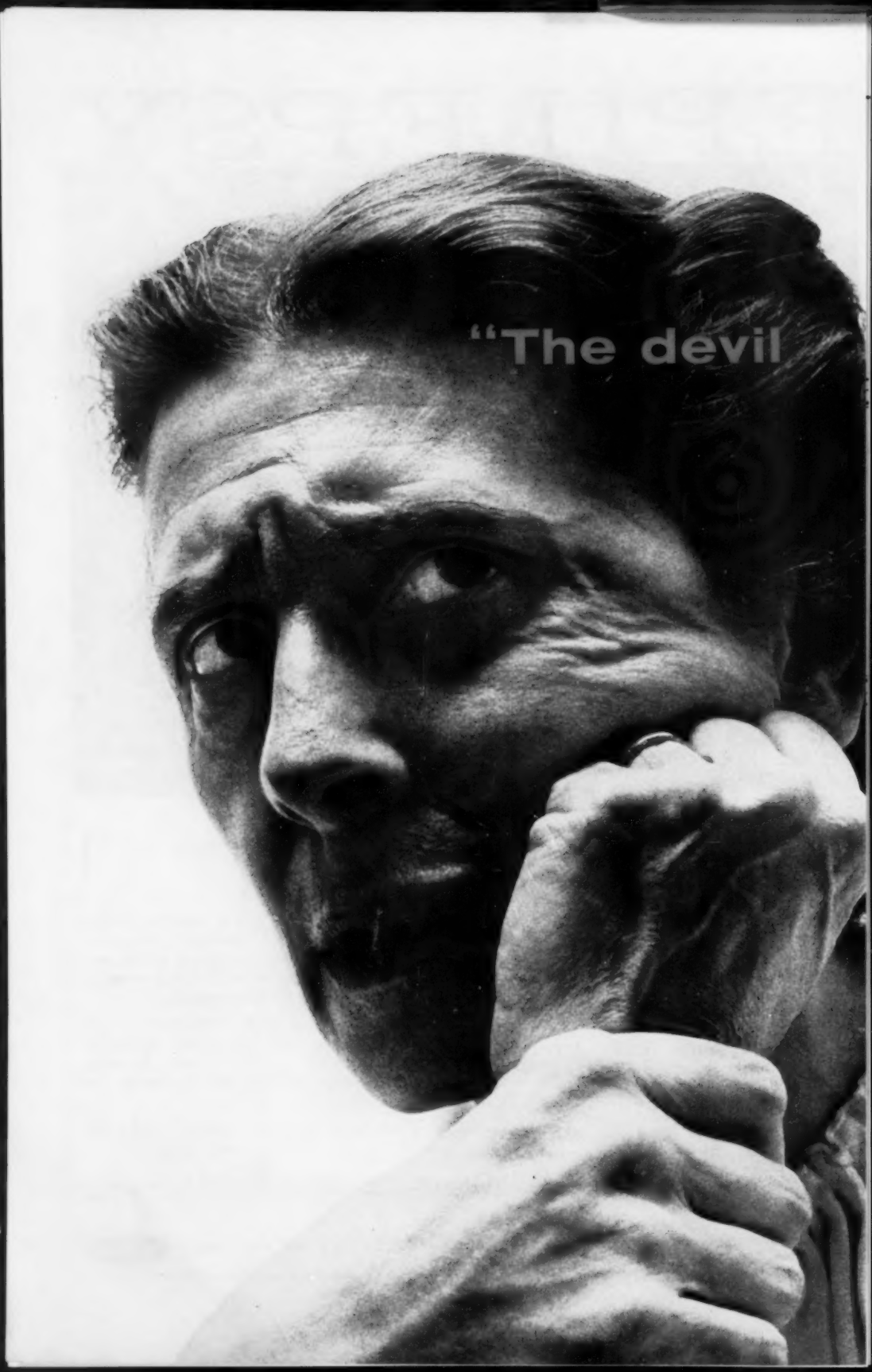
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1. Fazekas, J.F., et al.: J.A.M.A. *161*:46 (May 5) 1956.

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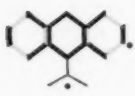

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